ABSTRACT

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SYNTHESIS AND CHARACTERIZATION OF BROMO AND CHLORO BENZALKONIUM SALTS AS POTENTIAL ANTIMICROBIAL COMPOUNDS

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Benzalkonium salts are recognized as among the best antiseptic ingredients. They are extensively utilized as preservatives and antibacterial agents and are usually found in household and industrial products. Quaternary ammonium compounds (QACs) are also used as antimicrobials in hospitals. Benzalkonium chlorides and bromides are primary components of QAC salts. Benzalkonium halides are generally used as disinfectants with a broad spectrum of antimicrobial impact. The purpose of this study was to synthesize and characterize new benzalkonium salts. The new benzalkonium salts were synthesized in a two-step reaction and characterized by proton nuclear magnetic resonance (^{1}H NMR), Fourier-transform infrared spectroscopy (FT-IR), and thermogravimetric analysis (TGA). Future research includes the testing of the compounds for antibacterial activity. The successful outcome of these studies will lead to further understanding of the structure property and activity relationships of the antimicrobial functions of benzalkonium salts.

SYNTHESIS AND CHARACTERIZATION OF BROMO AND CHLORO BENZALKONIUM SALTS AS POTENTIAL ANTIMICROBIAL COMPOUNDS

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TABLE OF CONTENTS

ACKNOWLEDGEMENTS ii

LIST OF FIGURES vi

LIST OF TABLES viii

LIST OF SCHEMES x

LIST OF ABBREVIATIONS xii

CHAPTER

I. INTRODUCTION 1

1.1 Benzalkonium Salts as Antibiotics 2

1.2 Susceptibility of Microorganisms to Benzalkonium Salts 2

1.3 Objective of Research 3

II. EXPERIMENTAL 4

2.1 Materials and Methods 4

2.2 Synthesis of 1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol (Compound A1) 5

2.3 Synthesis of (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol) (Compound B1-Br) 5

2.4 Synthesis of (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol) (Compound B1-Cl) 6

2.5 Synthesis of (1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl) amino)propan-2-ol) (Compound A2) 7

2.6 Synthesis of (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl) ammonium bromo)propan-2-ol) (Compound B2-Br) 8

2.7 Synthesis of (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl) ammonium chloro)propan-2-ol) (Compound B2-Cl) 9

CHAPTER

2.8 Synthesis of (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) (Compound A3) 10

2.9 Synthesis of (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) (Compound B3-Br) 10

2.10 Synthesis of (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) (Compound B3-Cl).....11

III. RESULTS AND DISCUSSION 13

3.1 Reactions..... 13

3.1.1 Compound A1 13

3.1.2 Compound B1-Cl.....14

3.1.3 Compound B1-Br.....15

3.1.4 Compound A2..... 16

3.1.5 Compound B2-Cl..... 17

3.1.6 Compound B2-Br..... 18

3.1.7 Compound A3.....19

3.1.8 Compound B3-Br..... 20

3.1.9 Compound B3-Cl..... 21

3.2 Characterization 22

3.2.1 Characterization of Compounds A1, B1-Br, and B1-Cl..... 22

3.2.2 Characterization of Compounds A2, B2-Br, and B2-Cl..... 33

3.2.3 Characterization of Compounds A3, B3-Br, and B3-Cl..... 45

3.3 Thin Layer Chromatography..... 59

CHAPTER

3.4 Reaction Mechanism of Compounds 60

3.4.1 Mechanism of the Synthesis of Compound A1, by Nucleophilic Addition Reaction 60

3.4.2 Mechanism of the Synthesis of Compound B1, a Bimolecular Substitution Nucleophilic (S_N2) Reaction 61

3.4.3 Mechanism of the Synthesis of Compound A2, by Nucleophilic Addition Reaction 62

3.4.4 Mechanism of the Synthesis of Compound B2, a Bimolecular Substitution Nucleophilic (S_N2) Reaction 63

3.4.5 Mechanism of the Synthesis of Compound A3, by Nucleophilic Addition Reaction 64

3.4.6 Mechanism of the Synthesis of Compound B3, a Bimolecular Substitution Nucleophilic (S_N2) Reaction 65

IV. CONCLUSION..... 66

REFERENCES 68

LIST OF FIGURES

Figure

1. General chemical structure of benzalkonium chlorides 2

2. 400 MHz ^{1}H NMR spectrum of compound A1(1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) in $CDCl_3$ 22

3. 400 MHz ^{1}H NMR spectrum of compound B1-Br (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol) in $CDCl_3$.....24

4. 400 MHz ^{1}H NMR spectrum of compound B1-Cl (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol)in $CDCl_3$ 26

5. Simulation ^{1}H NMR spectra of compound A1 and B1-X (X= Br, Cl) 28

6. FT-IR spectrum of compound A1(1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) 29

7. FT-IR spectrum of compound B1-Br (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol) 31

8. FT-IR spectrum of compound B1-Cl (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol).....32

9. 400 MHz ^{1}H NMR spectrum of compound A2 (1-(4-nonylphenoxy)-3-(N-benzyl-N((S)-1-phenylethyl)amino)propan-2-ol) in $CDCl_3$.....34

10. 400 MHz ^{1}H NMR spectrum of compound B2- Br (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol) in $CDCl_3$ 36

11. 400MHz ^{1}H NMR spectrum of compound B2-Cl (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol) in $CDCl_3$ 38

12. Simulation^{1}H NMR spectra of compound A2 and B2-X (X= Br, Cl) 40

13. FT-IR spectrum of compound A2 (1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol 41

Figure

14. FT-IR spectrum of compound B2-Br (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol) 43

15. FT-IR spectrum of compound B2-Cl (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol) 44

16. 400 MHz ^{1}H NMR spectrum of compound A3(1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) in $CDCl_3$ 46

17. 400 MHz ^{1}H NMR spectrum of compound B3-Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) in $CDCl_3$ 48

18. 400 MHz ^{1}H NMR spectrum of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) in $CDCl_3$ 50

19. Simulation ^{1}H NMR spectra of compound A3 and B3-X (X= Br, Cl) 53

20. FT-IR spectrum of compound A3(1-(3-nonylphenoxy)-3-(N-(2, 4-dinitrophenyl)-N- phenylamino)propan-2-ol) 54

21. FT-IR spectrum of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) 55

22. FT-IR spectrum of compound B3-Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) 57

23. TGA thermogram of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) 58

24. TGA thermogram of compound B3-Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) 58

25. TLC plate under UV light for compounds B2-Br, B1-Br, B3-Cl, B1-Cl, B2-Cl and B3-Br 59

LIST OF TABLES

Table

1. Observed ^{1}H NMR Chemical Shifts for Compound A1 (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) 23

2. Observed ^{1}H NMR Chemical Shifts for Compound B1-Br (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol) 25

3. Observed ^{1}H NMR Chemical Shifts for Compound B1-Cl (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol) 27

4. Summary of FT-IR Spectral Data for Compound A1 (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) 30

5. Summary of FT-IR Spectral Data for Compound B1-Br (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol)..... 31

6. Summary of FT-IR Spectral Data for Compound B1-Cl (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol)..... 33

7. Observed ^{1}H NMR Chemical Shifts for Compound A2 (1-(4-Nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol) 35

8. Observed ^{1}H NMR Chemical Shifts for Compound B2-Br (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo) propan-2-ol)..... 37

9. Observed ^{1}H NMR Chemical Shifts for Compound B2-Cl (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro) propan-2-ol)..... 39

10. Summary of FT-IR Spectral Data for Compound A2 (1-(4-Nonylphenoxy)-3-(N-benzyl- N-((S)-1-phenylethyl)amino)propan-2-ol) 42

11. Summary of FT-IR Spectral Data for Compound B2-Br (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol)..... 43

Table

12. Summary of FT-IR Spectral Data for Compound B2-Cl (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro) propan-2-ol) 45

13. Observed ^{1}H NMR Chemical Shifts for Compound A3 (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) 47

14. Observed ^{1}H NMR Chemical Shifts for Compound B3-Br (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo) propan-2-ol) 49

15. Observed ^{1}H NMR Chemical Shifts for Compound B3-Cl (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro) propan-2-ol) 51

16. Summary of FT-IR Spectral Data for Compound A3 (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) 54

17. Summary of FT-IR Spectral Data for Compound B3-Cl (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) 56

18. Summary of FT-IR Spectral Data for Compound B3-Br (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo) propan-2-ol) 57

LIST OF SCHEMES

Scheme

1. Synthesis of compound A1(of 1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) by nucleophilic addition reaction..... 13

2. Synthesis of compound B1-Cl (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol) by Menschutkin reaction (S_N2) 14

3. Synthesis of compound B1- Br (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethyliperidinium bromo-1-yl)propan-2-ol) by Menschutkin reaction (S_N2) 15

4. Synthesis of compound A2 (1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol) by nucleophilic addition reaction 16

5. Synthesis of compound B2 -Cl (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol) by Menschutkin reaction (S_N2) 17

6. Synthesis of compound B2-Br (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol by Menschutkin reaction (S_N2)) 18

7. Synthesis of compound A3 (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) by nucleophilic addition reaction.....19

8. Synthesis of compound B3 -Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) by Menschutkin reaction (S_N2) 20

9. Synthesis of compound B3 -Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) by Menschutkin reaction (S_N2) 21

10. Mechanism of the synthesis of compound A1, by nucleophilic addition reaction 60

11. Mechanism of the synthesis of compound B1, a bimolecular substitution nucleophilic (S_N2) reaction.....61

12. Mechanism of the synthesis of compound A2, by nucleophilic addition reaction 62

Scheme

13. Mechanism of the synthesis of compound B2, a bimolecular substitution nucleophilic (S_N2) reaction.....63

14. Mechanism of the synthesis of compound A3, by nucleophilic addition reaction 64

15. Mechanism of the synthesis of compound B3, a bimolecular substitution nucleophilic (S_N2) reaction.....65

LIST OF ABBREVIATIONS

QACs	Quaternary Ammonium Compounds
NMR	Nuclear Magnetic Resonance Spectroscopy
FT-IR	Fourier Transform Infrared Spectroscopy
TLC	Thin Layer Chromatography
SAR	Structure Activity Relationships
BAC	Benzalkonium Chloride
FDA	Food and Drug Administration
HIV	Human Immunodeficiency Virus
OTC	Over-the-counter

CHAPTER I

INTRODUCTION

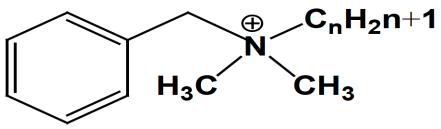
Generally, antibiotics are drugs or medications that slow the growth of bacteria. They consist of a range of medications that can save many lives if utilized properly. Antibiotics work by either stopping the bacteria from reforming or destroying it completely. The overuse of antibiotics has raised significant concern for medical professionals. This overuse and misuse of antibiotics contributes to the buildup of infections that are becoming resistant to the medical antibiotics.

Since antibiotics either destroy or stop bacteria from multiplying, there are several types that work in either of the following ways; a bactericidal antibiotic, interferes with the cell constituents or the actual formation of the bacterial cell wall and kills the bacteria; or a bacteriostatic, prevents the bacteria from reforming. Individuals who use antibiotics, such as penicillins, may develop allergic reactions to the drugs.[1]

Bacteria are the causes of many sorts of diseases. Development of resistance of bacteria against antibiotics is a serious issue. Bacteria develop different types of mechanisms in their functionality; chemical or biological nature of their cells that make them resistant against certain types of antibiotics.[2] This is a serious issue because resistance makes the antibiotics less effective. Thus, researchers are developing antibiotics that are effective against mutated disease-causing bacteria, including benzalkonium salts.[2]

1.1 Benzalkonium Salts as Antibiotics

Benzalkonium salts that are effective against bacteria are usually salt of quaternary ammonium compound (QACs). Since the 1930s, quaternary ammonium compounds have been broadly utilized to inhibit bacterial growth in clinical and industrial environments.[3] The surfactant properties of QACs make them effective against various types of bacteria.[4] Benzalkonium chlorides (BAC) are some of the most important QACs in use and are often used as preservatives in hospitals and health centers for pharmaceutical preparations and disinfectants (Figure 1).[5] Benzalkonium chlorides (BAC) are classified as category III active ingredient antiseptic by the United States Food and Drug Administration (US FDA). Category III antiseptics ingredients, such as, benzalkonium chloride, benzethonium chloride, chloroxylenol, ethyl alcohol, isopropyl alcohol, and povidone-iodine are most commonly used in over-the-counter (OTC) healthcare antiseptic products for which insufficient data is available to permit final classification.[6]



n = 8, 10, 12,14, 16, 18

Figure 1. General chemical structure of benzalkonium chlorides.

1.2 Susceptibility of Microorganisms to Benzalkonium Salts

Many types of gram-positive bacteria are susceptible towards the antibacterial activity of benzalkonium salt, such as, benzalkonium chloride (BAC). Gram-positive

bacteria contain negatively charged peptidoglycan and teichoic acids in their membranes.[7] The lack of permeability in membranes of these types of bacteria allows the BAC to be uptaken by bacteria and thus, cause the death of the bacteria.[8] Benzalkonium chloride is more effective against gram-positive than gram-negative bacteria, except Bacillus cereus because of its ability to form spores.[9] The most important benefits of benzalkonium salts as anti-pathogenic agents are that they are also effective in controlling the growth and development of many sorts of viruses. For example, BAC is effective against the Human Immunodeficiency Virus (HIV), Vaccinia virus, virus causing rabies disease, and feline pneumonitis virus.[10]

1.3 Objective of Research

The goal of this research is to synthesize and characterize benzalkonium salts for potential applications as bactericidal and bacteriostatic antibiotics. These compounds are expected to have good thermal stability, easy to synthesize at reduced cost, and have low toxicity. The compounds could be effective against gram-negative bacteria and gram-positive bacteria. Future work will reveal the efficacy of these new compounds against bacteria.

CHAPTER II

EXPERIMENTAL

2.1 Materials and Methods

Glycidyl-4-Nonylphenyl ether ($C_{18}H_{28}O_2$) (98 %), (*R*)-(+)-*N*-benzyl-α-methylbenzylamine ($C_{15}H_{17}N$) (98 %), and *cis*-2,6-dimethylpiperidine 2,4-dinitrodiphenyl amine ($C_{12}H_9N_3O_4$) (98 %) were obtained from Aldrich Chemical Company and used as received. Ethanol (500 ml, 99.5 %) was placed in one necked bottom flask, magnesium metal (98 %) (1.00 g), and iodine (99.8 %) (5.00×10^{-1} g) were added and the mixture was refluxed at 78 °C for 6 hours. The mixture was distilled to give pure ethanol and was used immediately. A Bruker AVANCE 400 MHZ spectrometer was used to obtain proton nuclear magnetic spectra. The standard internal resonance of the ^1H NMR was $CDCl_3$ at 7.24 ppm. A Perkin-Elmer Spectrum 65 FT-IR spectrometer was used to record IR spectra. All FT-IR of compound B samples were recorded using KBr pellets and compounds A FT-IR were obtained using Nujol® mull. The temperatures of the decomposition of the compounds were measured using TA-Instruments Q50 thermal analyser. Samples were mounted in platinum panels and deteriorated at a heating level of 10 °C/min under nitrogen gas atmosphere. The samples were heated to up 500 °C from room temperature. Thin layer chromatography was conducted using TLC silica gel

60F245-25 using methanol, ethyl ether or hexane as the mobile phase. Silica G prep TLC plates were viewed by UV54 indicator lamp (254 nm, 115 V60 HZ, 0.16 Amps).

2.2 Synthesis of 1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol (Compound A1)

In a single necked round bottom flask fitted with a condenser, glycidyl 4-Nonylphenyl ether (3.00×10^{-3} mol, 0.850 g) in dry ethanol (100 ml) was mixed with an equimolar amount of *cis*-2,6-dimethyl piperidine (3.00×10^{-3}, 0.339 g). Nitrogen gas was passed through the condenser for one hour, and the reaction mixture was refluxed for 24 hours using an oil bath to yield crude A1. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH 0.96 (t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01 (d, 1H, $(CCHCH)_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 2.63-2.38 (d, 2H, NCH_2CH) 1.90 (s, 1H, OH) 1.10 (t, 3H, $(CH_3CH_2)_2$) 2.41 (t, 1H, NCHCH2)$_2$) 1.55-1.45 (m, 2H, $CH_2CH_2CH_2)_2$) 1.59-1.34 (m, 2H, $CH_2CH_2CH_2$). FT-IR (Nujol®) 3348 br (OH), 1049 s (C-O-C), 1455 m (Ar C=C), 1290 w (N-C), 2973 m (Ar C-H), 803(Ar-*para*).

2.3 Synthesis of (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo -1-yl)propan-2-ol) (Compound B1-Br)

Benzyl bromide (3.00×10^{-3} mol, 0.345 g) was injected into the flask containing 1-(4-nonylphenoxy)-3-(2,6-dimethylpiperidin-1-yl)propan-2-ol, compound A1. The mixture was refluxed for 24 hours. The solvent was removed using a rotavapor. Fractions the of residue were collected and analyzed by TLC. The remainder of the residue was placed in a vacuum oven for 3 days at room temperature to dry. Purification of crude

compound B1was achieved using column chromatography using ethyl ether as the eluent. Then TLC was done to confirm the purity of compound using solvent mixtures of ethyl acetate and hexane in ratios of 1:1, followed by 1:5 and finally 1:8. The product was a colorless viscous liquid and obtained in 73.8 % yield. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH 0.96 (t, 3H, CH_3) 1.29 (m,12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01 (d,1H, $(CCHCH)_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.52 -3.27 (d, 2H, NCH_2CH) 2.40 (s, 1H, OH) 7.06 (d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH) 4.50 (s, 2H, NCH_2C) 1.35 (t, 3H, $(CH_3CH_2)_2$) 3.74 (t, 1H, NCHCH2)$_2$) 1.82-1.74 (m, 2H, $CH_2CH_2CH_2)_2$) 1.34-1.24 (m, 2H, $CH_2CH_2CH_2$). FT-IR(KBr) 3407 br (OH), 1248 s (C-O-C), 1456 m (Ar C=C), 1291 w (N-C), 3039 m (Ar-C-H), 827(Ar-*para*), 750 (Ar-mono).

2.4 Synthesis of (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol) (Compound B1-Cl)

Benzyl chloride (3.00×10^{-3} mol, 0.345 g) was injected into the flask containing 1-(4-Nonylphenoxy)-3-(2,6-dimethylpiperidin-1-yl)propan-2-ol, compound A1. The mixture was refluxed for 24 hours. The solvent was removed using a rotavapor. Fractions the of the residue were collected and analyzed by TLC. Then the reminder of the residue was placed in a vacuum oven for 3 days at room temperature to dry. Purification of crude compound B1was achieved with column chromatography using ethyl ether as a mobile phase. Then TLC was done to confirm the purity of compound, using solvent mixtures of ethyl acetate and hexane in ratios of 1:1, followed by 1:5 and finally 1:8. The product was

a colorless viscous liquid and obtained in 75.2 % yield. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH 0.96 (t,3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01 (d, 1H, $(CCHCH)_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.52 -3.27 (d, 2H, NCH_2CH) 2.40 (s, 1H, OH) 7.06 (d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH) 4.50 (s, 2H, NCH_2C) 1.35 (t, 3H, $(CH_3CH_2)_2$) 3.74 (t, 1H, NCHCH2)$_2$) 1.82-1.74 (m, 2H, $CH_2CH_2CH_2)_2$) 1.34-1.24 (m, 2H, $CH_2CH_2CH_2$) 4.05 (q, 1H, CH_3CHC) 1.63 (d, 3H, CH_3CHN). FT-IR (KBr) 3426 br (OH), 1246 s (C-O-C), 1456 m (Ar C=C), 1292 m (N-C), 828 (Ar-*para*), 3039 m (Ar C-H), 751 (Ar-mono).

2.5 Synthesis of (1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl) amino) propan-2-ol) (Compound A2)

In a single necked round bottom flask fitted with a condenser, glycidyl 4-nonylphenyl ether (3.00×10^{-3} mol, 0.850 g) in dry ethanol (100 ml) was mixed with an equimolar amount of (*R*)-(+)-*N*-Benzyl-α-methylbenzylamine (3.00×10^{-3} mol, 0.633 g). Nitrogen gas flowed through the condenser for one hour, and the reaction mixture was refluxed for 24 hours using an oil bath to yield compound A2. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400MHz): δH 0.96 (t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55(t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01 (d, 1H, $(CCHCH)_2$) 3.96 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 2.63-2.38 (d, 2H, NCH_2CH) 2.50 (s, 1H, OH) 7.06(d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH)) 7.21 (m, 1H, $(CHCHCH)_2$) 7.12 (d, 1H, $(CHCHC)_2$) 7.08 (m, 1H, CHCHCH) 4.08 (q, 1H,

CH3CHC) 1.38 (d, 3H, CH_3CHN). FT-IR (Nujol®) 3445 br (OH), 1246 s (C-O-C), 1448 m (Ar C=C), 1374 w (N-C), 2971 m (Ar C-H), 847(Ar-*para*).

2.6 Synthesis of (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl) ammonium bromo)propan-2-ol) (Compound B2-Br)

Benzyl bromide (3.00×10^{-3} mol, 0.345 g) was injected into a flask containing of 1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol, compound A2. The mixture was refluxed for 24 hours. The solvent was removed using a rotavapor. Fractions of residue were collected and analyzed by TLC. The remaining residue was placed in a vacuum oven for 3 days at room temperature to dry. Purification of crude compound B2 was achieved by silica G prep TLC plates using ethyl ether and hexane 1:1 as eluent. Then the silica of the stationary phase was the scraped-off and extracted by methanol and centrifuged. The liquid was removed by pipette, freeze-dried for 24 hours and the purity checked via TLC. The compound B2-Br was obtained as a colorless viscous in 74.3 % yield. ^{1}HNMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH 0.96 (t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01(d, 1H, $(CCHCH)_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.52-3.27 (d, 2H, NCH_2CH) 2.34 (s, 1H, OH) 7.06(d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH) 4.50 (s, 2H, CCH_2N) 7.06 (d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH) 7.21 (m, 1H, $(CHCHCH)_2$) 7.12 (d, 1H, $(CHCHC)_2$) 7.08 (m, 1H, CHCHCH) 5.03 (q, 1H, CH3CHC) 1.63 (d, 3H, CH_3CHN). FT-IR (KBr) 3437s (OH), 1247 m (N-C), 827 (Ar-*para*), 746 (Ar-mono), 1581,1511 s (Ar-C=C), 3028 s (Ar-C-H), 1186 s (C-O-C), 2959 w (Ar-C-H).

2.7 Synthesis of (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl) ammonium chloro)propan-2-ol) (Compound B2-Cl)

Benzyl chloride (3.00×10^{-3} mol, 0.345 g) was injected into the flask containing of 1-(4-Nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl) amino) propan-2-ol, compound A2. The mixture was refluxed for 24 hours. The solvent was removed using a rotavapor. Fractions of the residue were collected and analyzed by TLC. Then the reminder of the residue was placed in a vacuum oven for 3 days at room temperature to dry. Purification of crude compound B2 was achieved by silica G prep TLC plates using ethyl ether and hexane 1:1 as eluent. Then the silica of the stationary phase was scraped-off and extracted by methanol and centrifuged. The liquid was removed by pipette, freeze-dried for 24 hours and the purity checked via TLC. The compound B2-Br was obtained as a colorless viscous in 70.4 % yield. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH 0.96 (t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01(d, 1H, $(CCHCH)_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.52-3.27 (d, 2H, NCH_2CH) 1.90 (s, 1H, OH) 7.06 (d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH) 4.50 (s, 2H, CCH_2N) 7.06 (d, 1H, $(CHCHC)_2$) 7.14 (m, 1H, $(CHCHCH)_2$) 7.07 (m, 1H, (CHCHCH) 7.21 (m, 1H, $(CHCHCH)_2$) 7.12 (d, 1H, ($CHCHC)_2$) 7.08 (m, 1H, CHCHCH) 5.03 (q, 1H, CH3CHC) 1.63 (d, 3H, CH_3CHN). FT-IR (KBr) 3437 s (OH), 1247 m (N-C), 827 (Ar-*para*), 749 (Ar-mono), 1512 s (Ar-C=C), 2966 s (Ar-C-H), 1186 s (C-O-C).

2.8 Synthesis of (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) (Compound A3)

In a single necked round bottom flask fitted with a condenser, glycidyl 4-Nonylphenyl ether (3.00×10^{-3} mol, 0.850 g) in dry ethanol (100 ml) was mixed with an equimolar amount of 2,4-dinitrodiphenyl amine (3.00×10^{-3} mol, 0.776 g). Nitrogen gas was flowed through the condenser for one hour, and the reaction mixture was refluxed for 24 hours using an oil bath to yield A3. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH0.96 (t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, $(CHCHC)_2$) 7.01 (d, 1H, $(CCHCH)_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.34 -3.09 (d, 2H, NCH_2CH) 2.45 (s, 1H, OH) 7.04 (q, 1H, $(CH, CHCH)_2$) 6.43 (d, 1H, $(CCHCH)_2$) 6.58 (q, 1H, CHCHCH) 8.36 (d, 1H, CCHCH) 8.90 (s, 1H, CCHC). FT-IR (Nujol®) 3335 br (OH), 1050 s (C-O-C), 1455 m (Ar C=C), 1090 w (N-C), 2974 m (Ar C-H), 881(Ar-*para*).

2.9 Synthesis of (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) (Compound B3-Br)

Benzyl bromide (3.00×10^{-3} mol, 0.345 g) was injected into the flask containing 1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol, compound A3. The mixture was refluxed for 24 hours. The solvent was removed using a rotavapor. Fractions of the residue were collected and analyzed by TLC using ethyl acetate and hexane in ratios of 1:1, followed by 1:5 and finally 1:8. The orange product was obtained in 72.9 % yield. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz): δH 0.96(t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2CH_2) 6.72 (d, 1H,

(CHCHC)$_2$) 7.01(d, 1H, (CCHCH)$_2$) 4.35 (m,1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.61 -3.36 (d, 2H, NCH_2CH) 2.50 (s, 1H, OH) 7.62 (q, 1H, (CHCHCH)$_2$) 7.57 (q, 1H, (CHCHCH)$_2$) 7.95 (d, 1H, (CCHCH)$_2$) 4.59 (s, 2H, NCH_2CH)) 7.06 (d, 1H, (CHCHC)$_2$) 7. 14 (m, 1H, (CHCHCH)$_2$) 7.07 (m, 1H, (CHCHCH) 8.47 (d, 1H, CHCHC) 8.94 (d, 1H, CCHCH) 9.48 (s, (CCHC)). FT-IR (KBr) 3317s (OH), 1377 m (N-C), 825 (Ar-*para*), 692(Ar-mono), 1462 s (Ar-C=C), 3028 s (Ar-C-H), 1248 s (C-O-C), 2853 w (Ar-C-H).

2.10 Synthesis of (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) (Compound B3-Cl)

Benzyl chloride (3.00×10^{-3} mol, 0.345 g) was injected into the flask containing 1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol, compound A3. The mixture was refluxed for 24 hours. The solvent was removed using a rotavapor. Fractions of the residue was collected and analyzed by TLC using ethyl acetate and hexane in ratios of 1:1, followed by 1:5 and finally1:8. The orange product was obtained in 76.3 % yield. ^{1}H NMR ($CDCl_3$), with 0.7 % v/v TMS, 400 MHz):δH 0.96 (t, 3H, CH_3) 1.29 (m, 12H, $(CH_2)_5$) 1.62 (m, 2H, CH_2) 2.55 (t, 2H, Ar-CH_2 CH_2) 6.72 (d, 1H, (CHCHC)$_2$) 7.01 (d, 1H, (CCHCH)$_2$) 4.35 (m, 1H, CH_2CHCH_2) 4.22-3.97 (d, 1H, CHCHO) 3.61 -3.36 (d, 2H, NCH_2CH) 2.40 (s, 1H, OH) 7.62 (q, 1H, (CHCHCH)$_2$) 7.57 (q, 1H, (CHCHCH)$_2$) 7.95 (d, 1H, (CCHCH)$_2$) 4.59 (s, 2H, NCH_2CH)) 7.06 (d, 1H, (CHCHC)$_2$) 7.14 (m, 1H, (CHCHCH)$_2$) 7.07 (m, 1H, (CHCHCH) 8.47 (d, 1H, CHCHC) 8.94 (d, 1H,CCHCH) 9.48 (s, CCHC). FT-IR (KBr) 3435 s (OH), 1059 w (N-C),

1146 s (C-O-C), 749 (Ar-mono), 1518, 1337 s (NO_2), 825 (Ar-*para*), 1583 w (C=C), 2961 s (Ar-C-H).

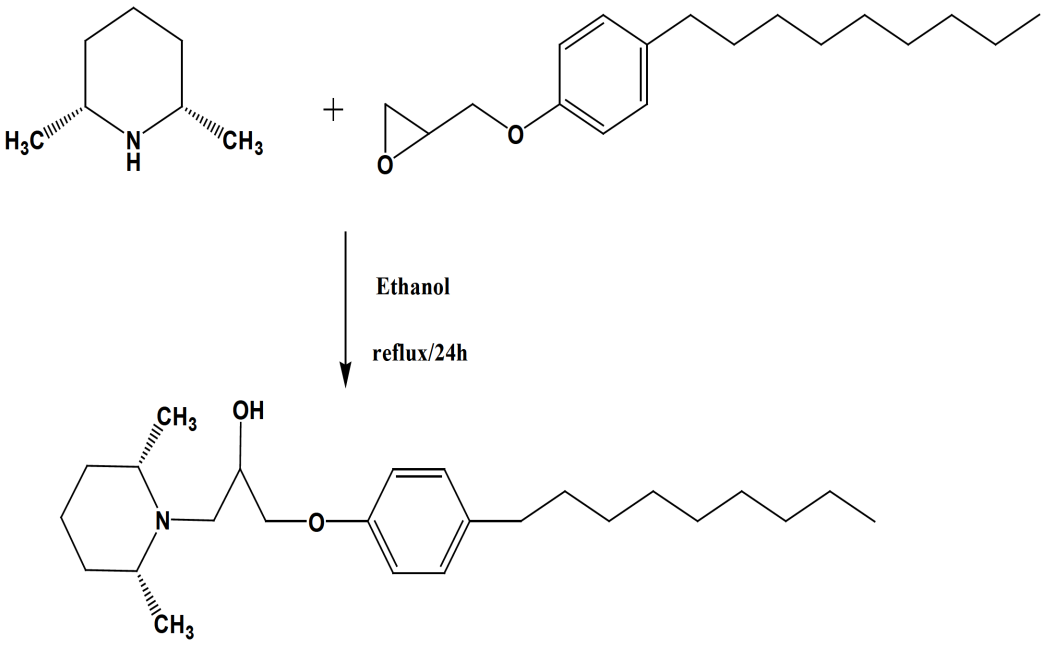
CHAPTER III

RESULTS AND DISCUSSION

3.1 Reactions

3.1.1 Compound A1

Scheme 1 shows the synthetic route to the preparation of compound A1 via a nucleophilic addition reaction. The compound was obtained in good yield. Compound A1 was characterized using FT-IR and ^{1}H NMR spectroscopy.

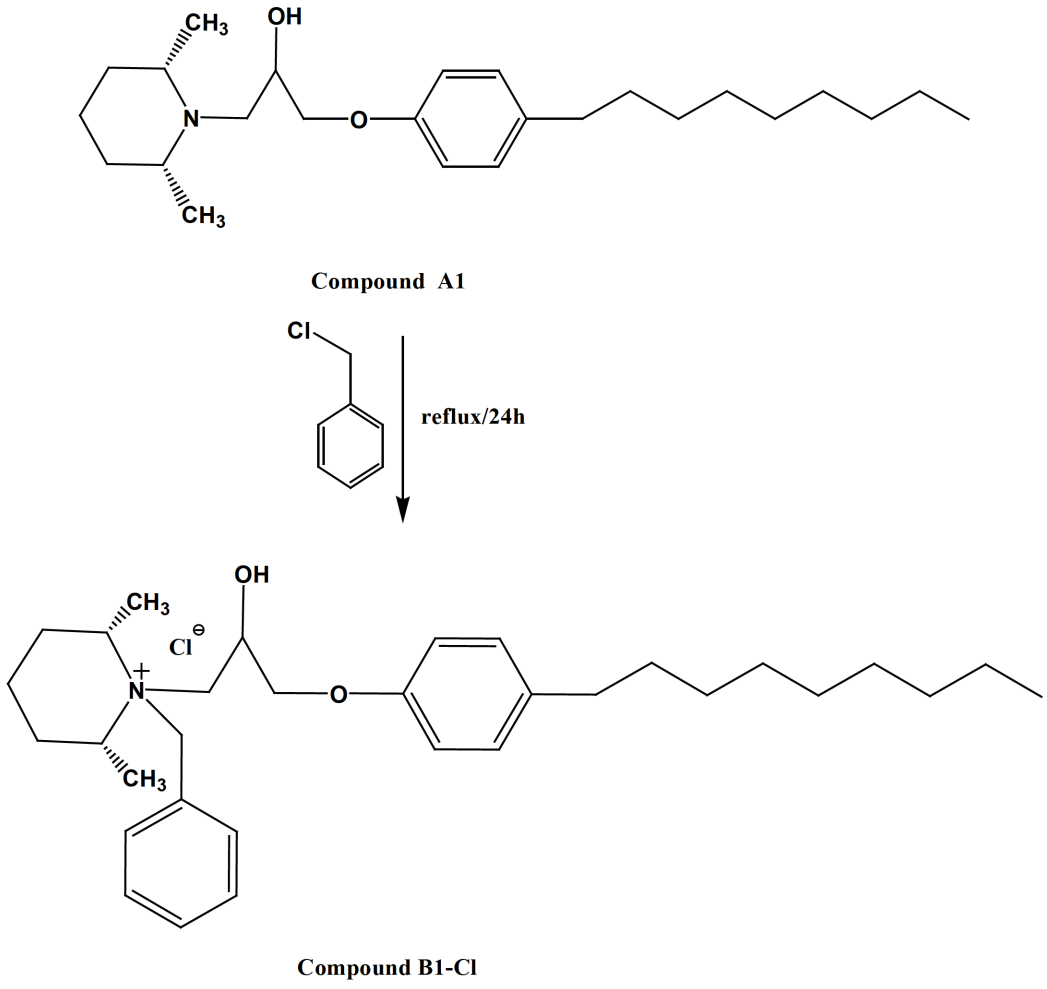


Compound A1

Scheme 1. Synthesis of compound A1 (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) by nucleophilic addition reaction.

3.1.2 Compound B1-Cl

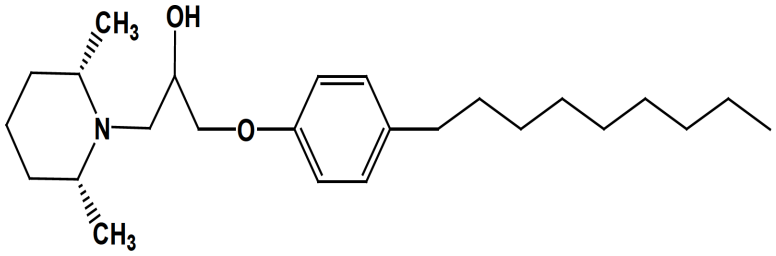
Scheme 2 shows the synthetic route to the preparation of compound B1-Cl via a nucleophilic addition reaction. The compound was obtained in good yield. Compound B1-Cl was characterized using FT-IR and ^{1}H NMR spectroscopy.



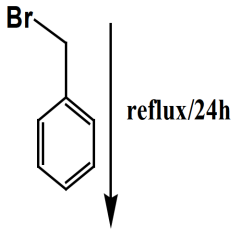
Scheme 2. Synthesis of compound B1-Cl (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol) by Menschutkin reaction (S_N2).

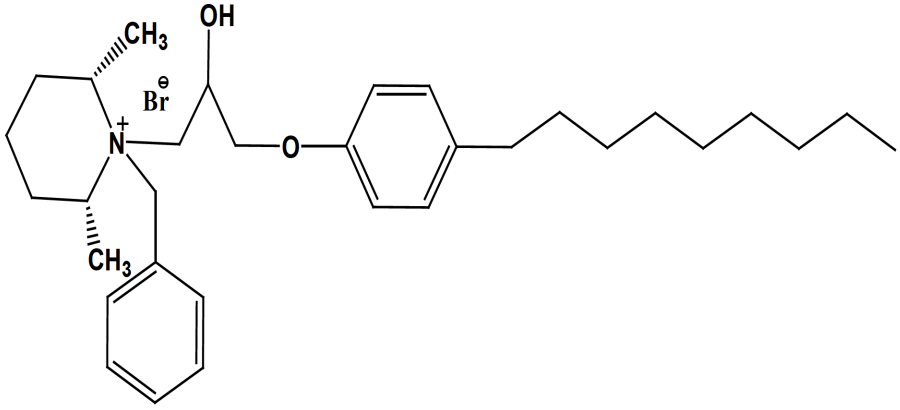
3.1.3 Compound B1-Br

Scheme 3 shows the synthetic route to the preparation of compound B1-Br via a nucleophilic addition reaction. The compound was obtained in good yield. Compound B1-Br was characterized using FT-IR and ^{1}H NMR spectroscopy.



Compound A1



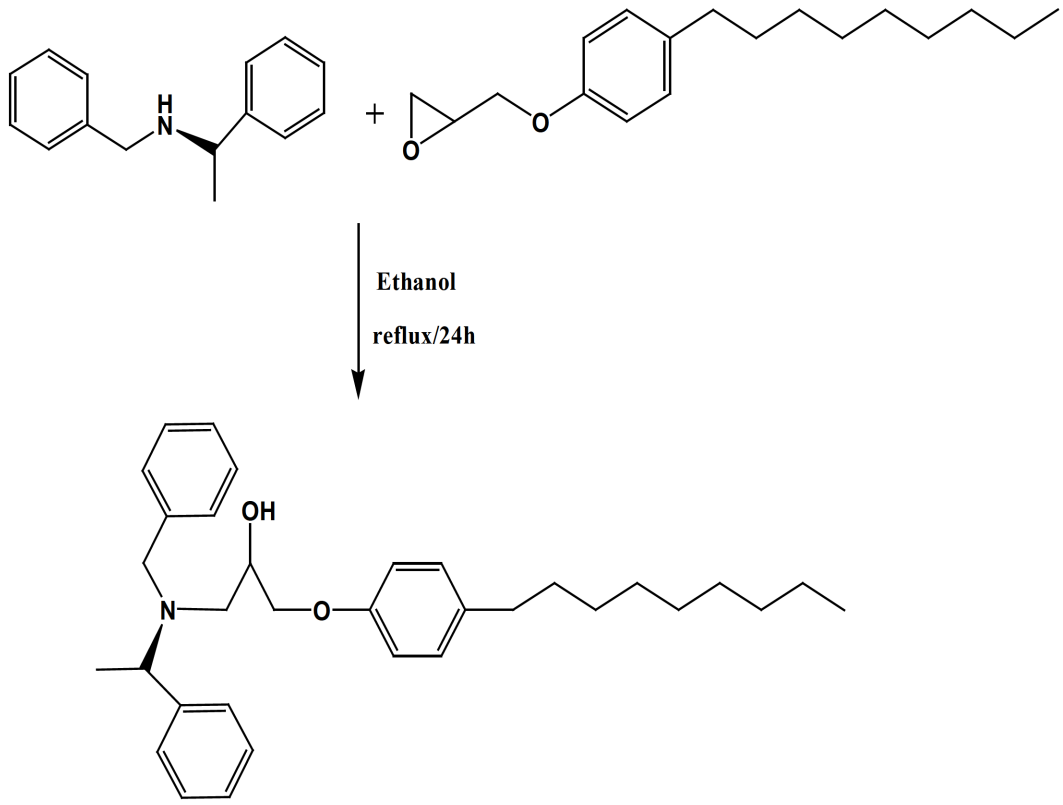


Compound B1-Br

Scheme 3. Synthesis of compound B1- Br (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol) by Menschutkin reaction (S_N2).

3.1.4 Compound A2

Scheme 4 shows synthetic route to the preparation of compound A2 via a nucleophilic addition reaction. The compound was obtained in good yield. Compound A2 was characterized using FT-IR, ^{1}H NMR spectroscopy.

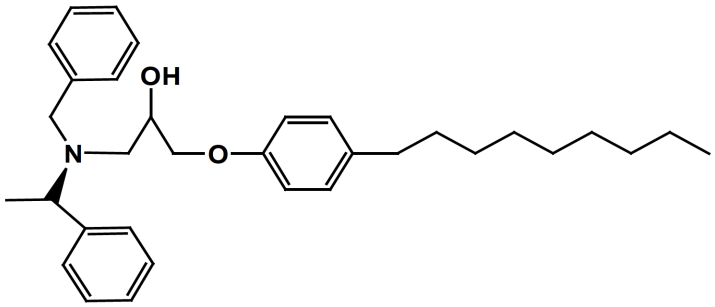


Compound A2

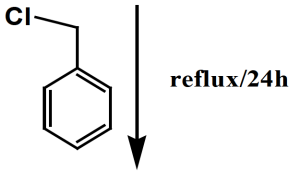
Scheme 4. Synthesis of compound A2 (1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol) by nucleophilic addition reaction.

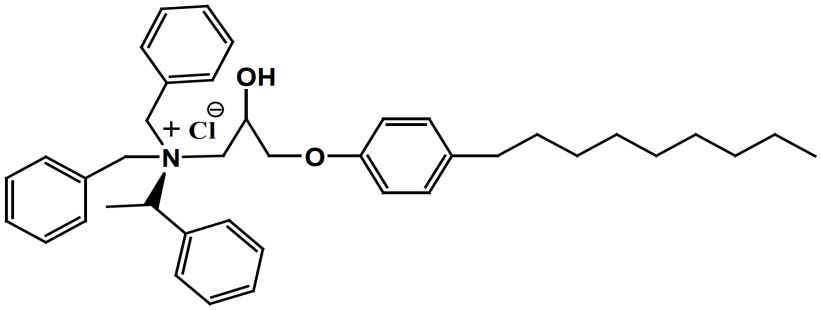
3.1.5 Compound B2-Cl

Scheme 5 shows the synthetic route to the preparation of compound B2-Cl via the nucleophilic addition reaction. The compound B2-Cl was obtained in good yield. Compound B2-Cl was characterized using FT-IR and ^{1}H NMR spectroscopy.



Compound A2



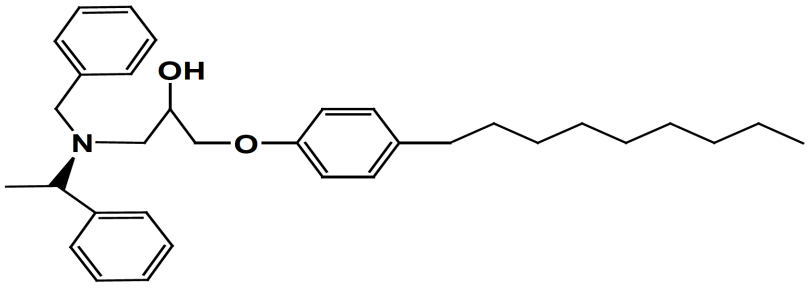


Compound B2-Cl

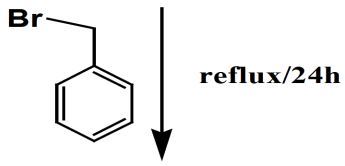
Scheme 5. Synthesis of compound B2 -Cl (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol) by Menschutkin reaction (S_N2).

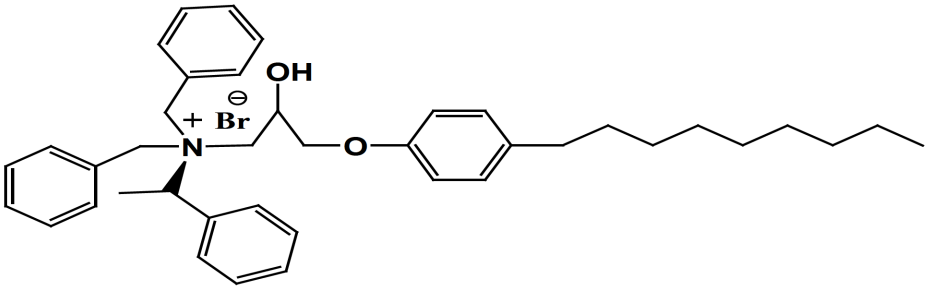
3.1.6 Compound B2-Br

Scheme 6 shows the synthetic route to the preparation of compound B2-Br via a nucleophilic addition reaction. The compound B2-Br was obtained in good yield and characterized using FT-IR and ^{1}H NMR spectroscopy.



Compound A2



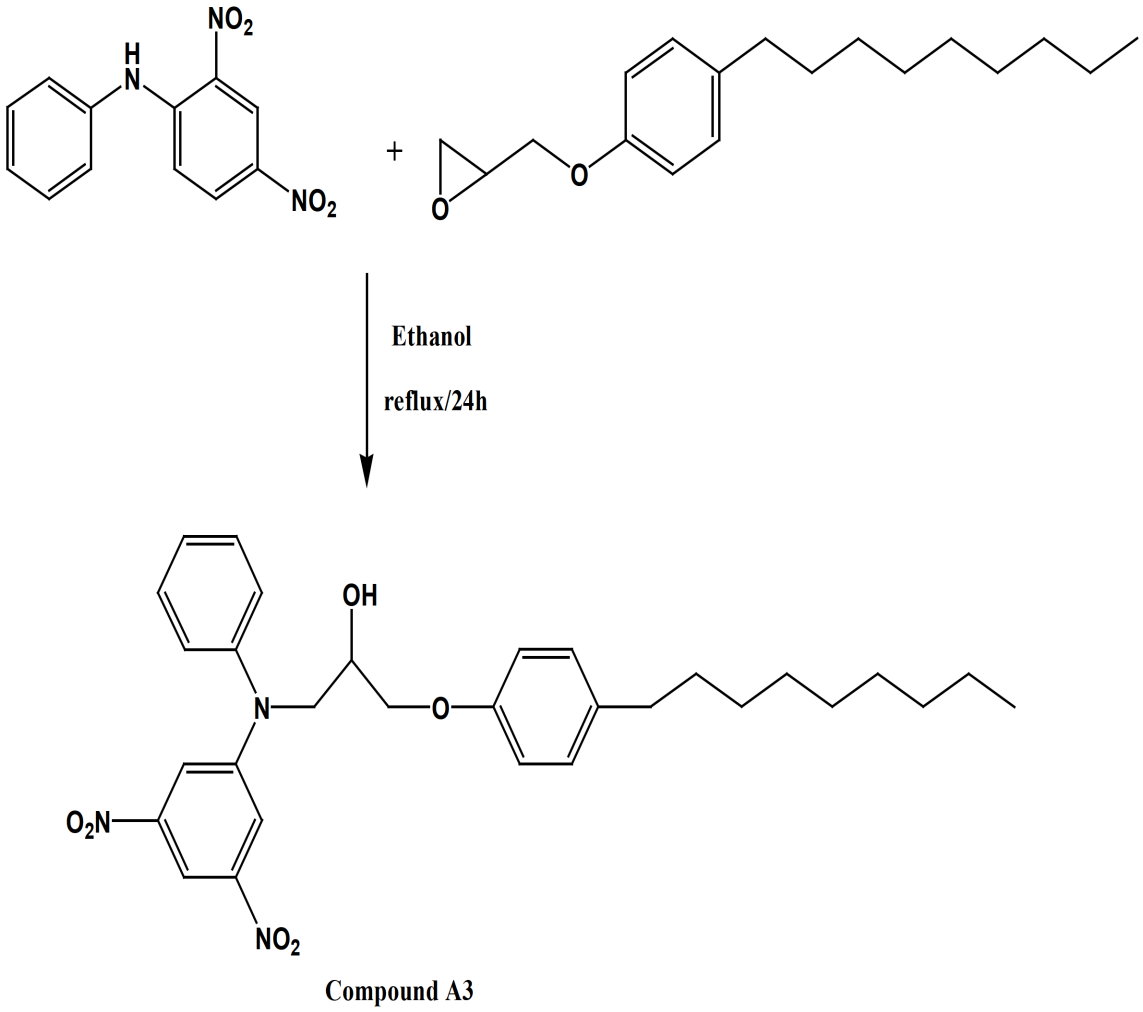


Compound B2-Br

Scheme 6. Synthesis of compound B2-Br (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol) by Menschutkin reaction (S_N2).

3.1.7 Compound A3

Scheme 7 shows the synthetic route to the preparation of compound A3 via a nucleophilic addition reaction. The compound was obtained in good yield. Compound A3 was characterized using FT-IR and ^{1}H NMR spectroscopy.

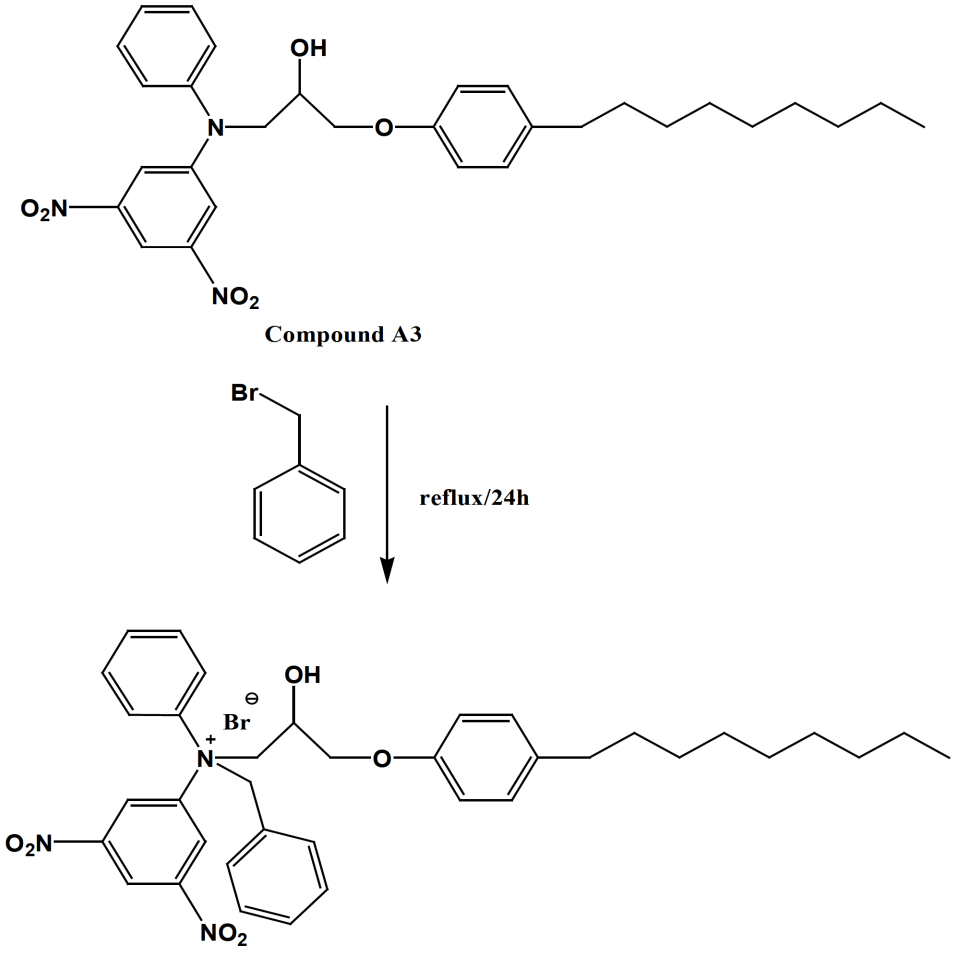


Compound A3

Scheme 7. Synthesis of compound A3 (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) by nucleophilic addition reaction.

3.1.8 Compound B3-Br

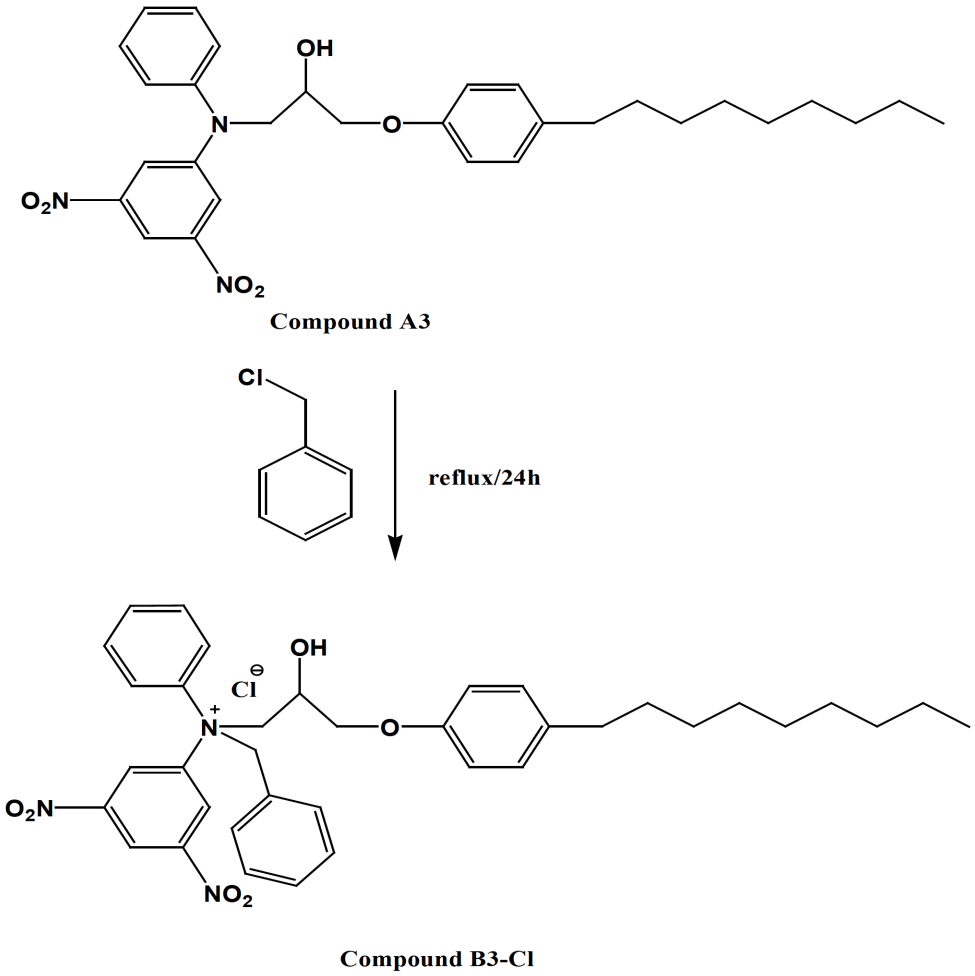
Scheme 8 shows the synthetic route to the preparation of compound B3-Br via a nucleophilic addition reaction. The compound B3-Br was obtained in good yield and characterized using FT-IR, TGA and ^{1}H NMR spectroscopy.



Scheme 8. Synthesis of compound B3 -Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) by Menschutkin reaction (S_N2).

3.1.9 Compound B3-Cl

Scheme 9 shows the of preparation compound B3-Cl via through a Menschutkin reaction (S_N2) after the addition of benzyl chloride. The purity was checked using thin layer chromatography. The structure was studied using the ^1H NMR, FT-IR, and the thermal stability analyzed by TGA techniques.



Scheme 9. Synthesis of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) by Menschutkin reaction (S_N2).

3.2 Characterization

3.2.1 Characterization of Compounds A1, B1-Br, and B1-Cl

^{1}H NMR spectra analysis confirmed the structures of compounds A1, B1-Br and B1-Cl. The ^{1}H NMR of compound A1 is displayed in Figure 2, and the peak assignments are presented in Table 1. The chemical shifts of the aromatic ring appear between 6.55 and 7.40 ppm. The spectrum showed the long alkyl chain chemical shifts (C_9H_{19}) in the 0.96 - 2.55 ppm region. The chemical shifts for the methylene proton attached to the nitrogen appears at 3.06 ppm.

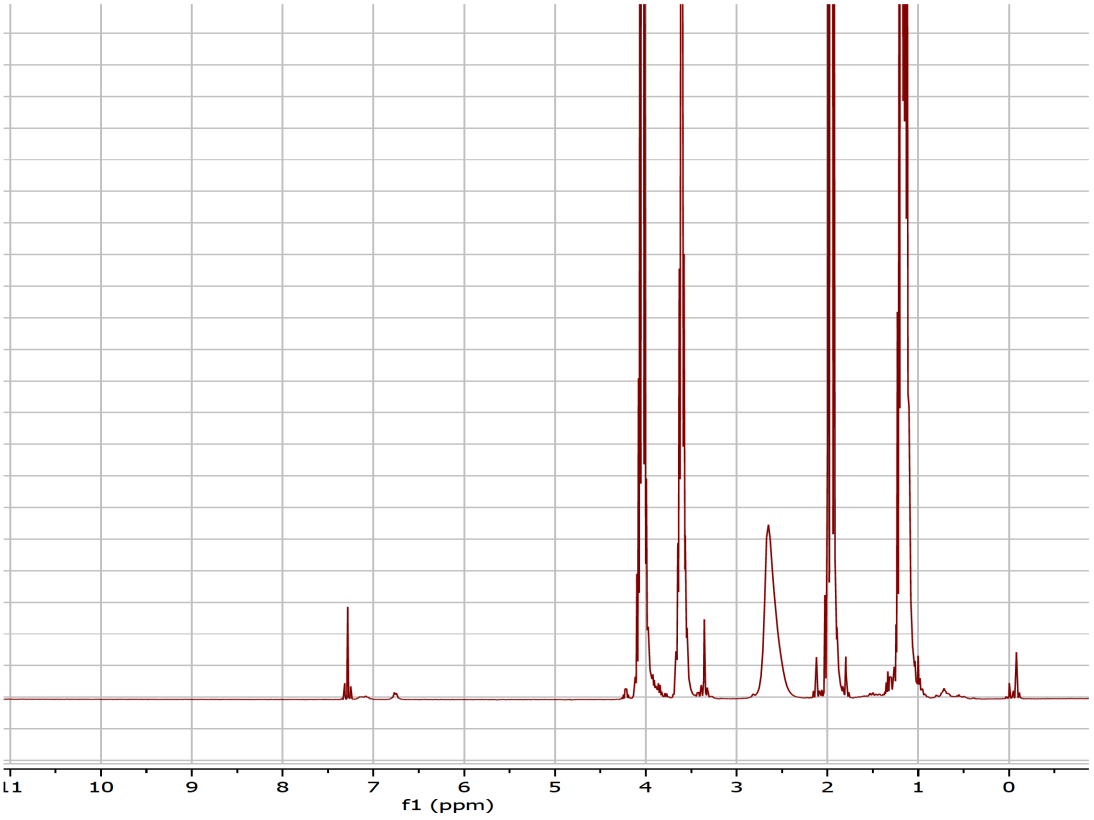
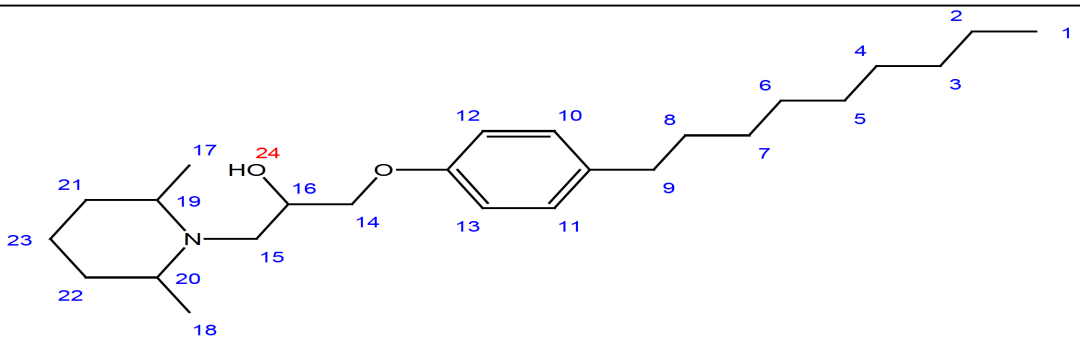


Figure 2. 400 MHz ^{1}H NMR spectrum of compound A1 (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) in $CDCl_3$.

Table 1. Observed ^{1}H NMR Chemical Shifts for Compound A1(1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol) in $CDCl_3$



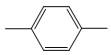
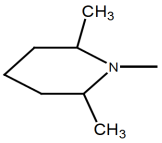
Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
CH	16	3.96	
CH_2	14	4.05	Doublet
	15	3.06	
OH	24	1.90	Alcohol
	10, 11	7.01	*para*-Aromatic
	12, 13	6.72	ring
	17, 18	1.10	Doublet
	19, 20	2.09	Doublet
	21, 21	2.18	Doublet
	23	1.45	

Figure 3 shows ^{1}H NMR spectrum of compound B1-Br and the peak assignments are presented in Table 2. The chemical shifts of the two aromatic rings appear between 6.27 and 7.14 ppm. The spectrum shows the long alkyl chain chemical shifts (C_9H_{19}) in the 0.96 - 2.55 ppm region. The chemical shifts for the methylene proton attached to the nitrogen atom appears at 4.53 ppm. The hydrogen of the hydroxide group appears at 2.90 ppm.

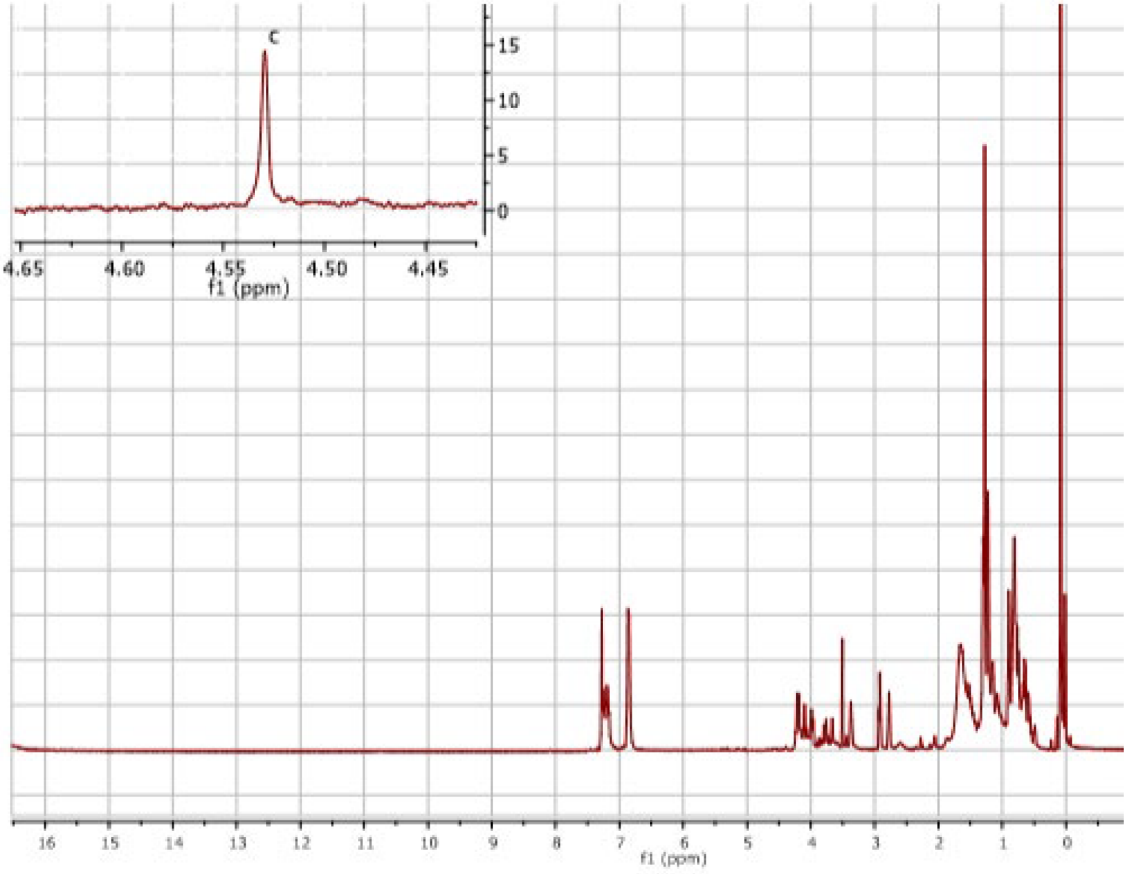
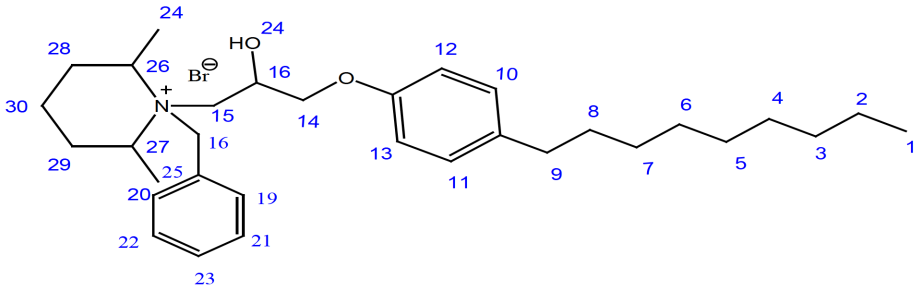


Figure 3. 400 MHz ^{1}H NMR spectrum of compound B1-Br (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol) in $CDCl_3$.

Table 2. Observed ^{1}H NMR Chemical Shifts for Compound B1-Br (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol)



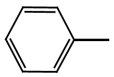
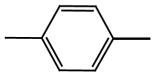
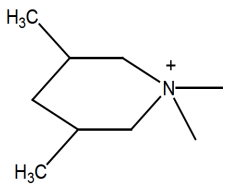
Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
CH	17	6.05	
CH_2	14	4.50	
	15	3.93	
	16	3.68	
OH	18	1.90	Alcohol
	19, 20	7.06	Mono-aromatic rings
	21, 22	7.14	
	23	7.07	
	11, 13	7.01	*para*-Aromatic ring
	10, 12	6.27	
	24, 25	1.06	Doublet
	26, 27	1.34	Doublet
	28, 29	3.33	Doublet
	30	3.08	

Figure 4 shows the ^{1}H NMR spectrum of compound B1-Cl, the peak assignments are presented in Table 3. The chemical shifts of the two aromatic rings appears between 6.27 and 7.14 ppm. The spectrum shows the long alkyl chain (C_9H_{19}) chemical shifts in the 0.96 - 2.55 ppm region. The methylene proton attached to the nitrogen atom appears at 4.54 ppm. The hydrogen attached to the hydroxide group appears at 1.90 ppm.

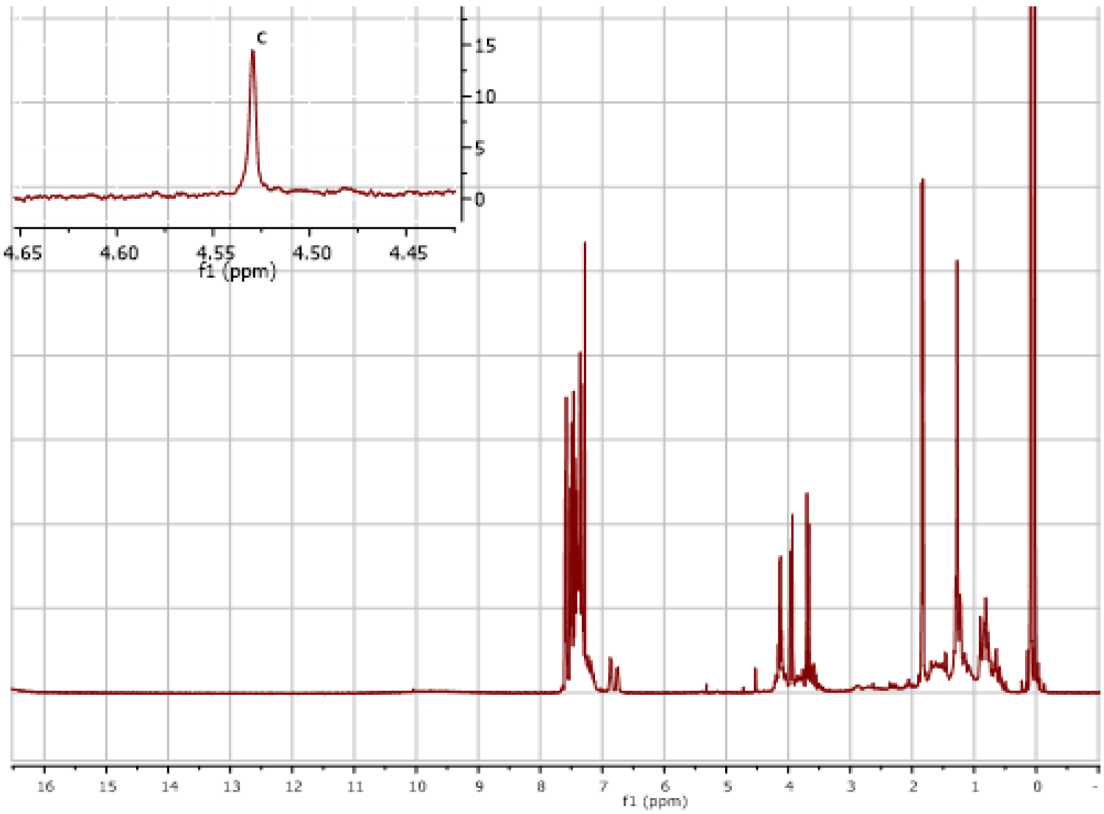
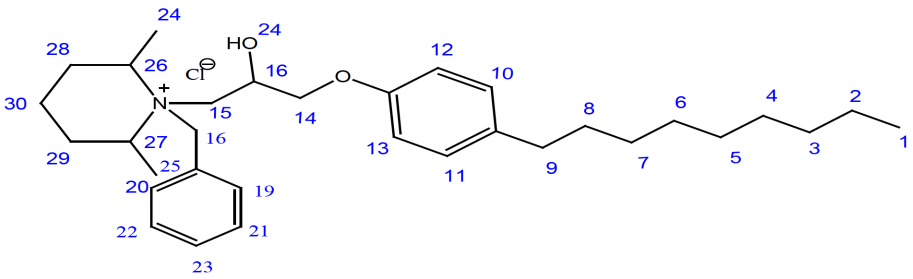


Figure 4. 400 MHz ^{1}H NMR spectrum of compound B1-Cl (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol) in $CDCl_3$.

Table 3. Observed ^{1}H NMR Chemical Shifts for Compound B1-Cl (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol)



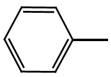
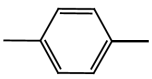
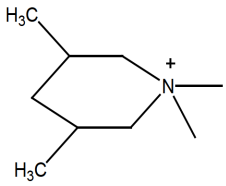
Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
CH	17	6.05	
CH_2	14	4.50	
	15	3.93	
	16	3.68	
OH	18	1.90	Alcohol
	19, 20	7.06	Mono-aromatic rings
	21, 22	7.14	
	23	7.07	
	11, 13	7.01	*para*-Aromatic ring
	10, 12	6.27	
	24, 25	1.06	Doublet
	26, 27	1.34	Doublet
	28, 29	3.33	Doublet
	30	3.08	

Figure 5 shows the comparison between the ^{1}H NMR spectra of compounds A1 and B1-X (X= Cl, Br). In the ^{1}H NMR spectrum of compound A1, the peak at 3.33 ppm corresponds to methylene protons linked to the nitrogen atom, the peak at 2.44 ppm corresponds to methine proton attached to nitrogen atom.

The ^{1}H NMR spectrum of compound B1-X shows chemical shifts evident of the protons located adjacent to the quaternary nitrogen atom of compound B1-X. The signal at 3.58 ppm corresponds to methylene protons linked to the nitrogen atom. The chemical shift at 2.96 ppm corresponds to methine proton attached to nitrogen atom. The methylene hydrogens of the carbon attached to nitrogen atom of compounds B1-Br and B1-Cl show signals at 4.53 and 4.54 ppm, respectively.

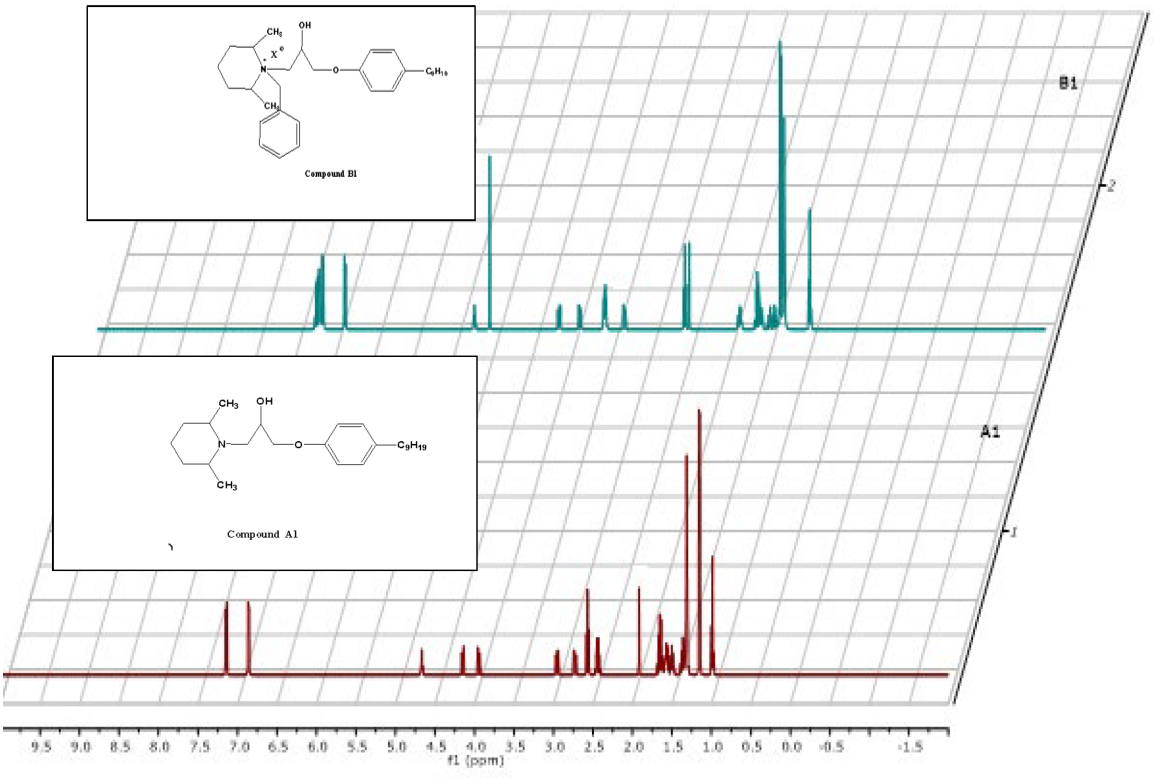


Figure 5. Simulation ^{1}H NMR spectra of compound A1 and B1-X (X= Br, Cl).

FT-IR spectrum shows the presence of the expected functional groups of compound A1, and is presented in Figure 6 and summarized in Table 4. The FT-IR spectrum shows a characteristic absorption band at 3459 cm^{-1} corresponding to OH stretching vibration. The C-N showed a sharp band at 1091 cm^{-1}. The peaks at 1741 and 1447 cm^{-1} are due to the bending of the aromatic C=C. The C-O-C band shows an absorption at 1243 cm^{-1}. The peak at 847 cm^{-1} is due to the *para* aromatic substituted absorption. The aromatic C-H appears at 2977 cm^{-1}.

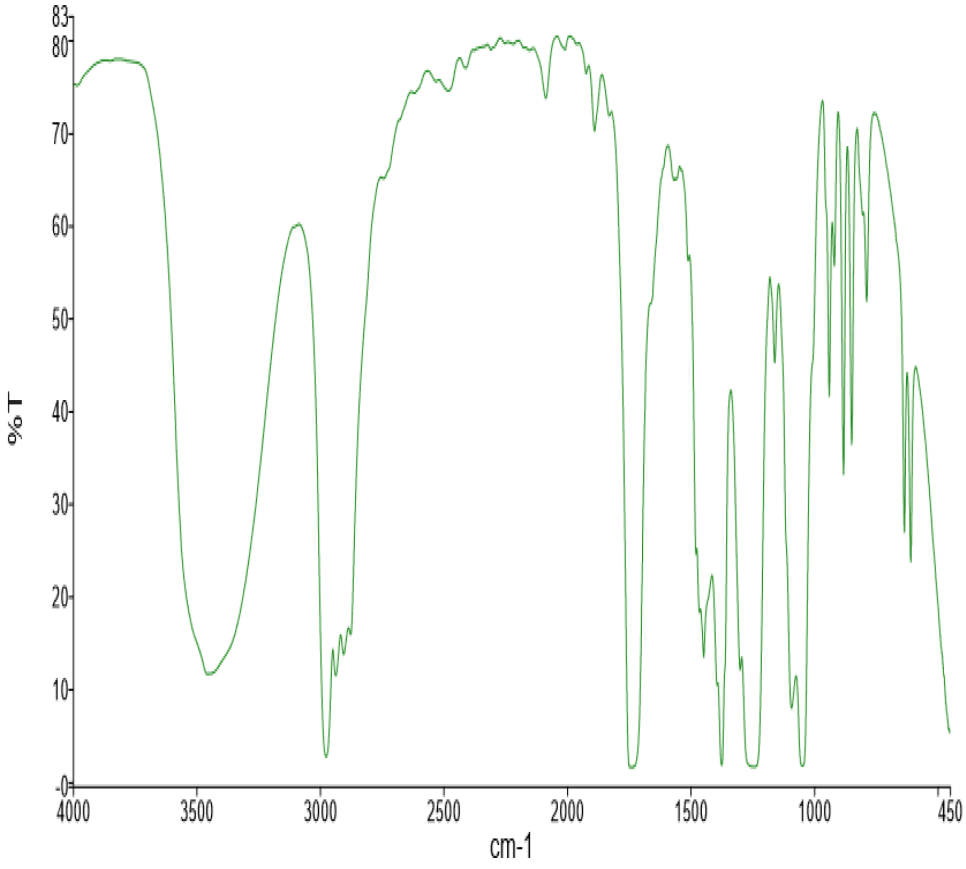


Figure 6. FT-IR spectrum of compound A1(1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol).

Table 4. Summary of FT-IR Spectral Data for Compound A1 (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidin-1-yl)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
O-H	3459	Strong
N-C	1091	Weak
C-O-C	1243	Strong
Ar-C=C	1447-1741	Weak, multiple bands, Strong
Ar-C-H	2977	Strong
Ar-*para*	847	

The FT-IR absorption peaks are consistent with the functional groups present in compound B1-Br. The broad OH stretching vibration absorption at 3407 cm^{-1}. The C-H stretch of alkyl chain appears at 3039 cm^{1}. The peak at 1741 and 1447 cm^{-1} are due to bending aromatic C=C. The C-O-C band appears at 1248 cm^{-1}. The peak at 750 cm^{-1} is due to the monosubstituted aromatic absorption. The peak at 827 cm^{-1} is due to *para* substituted aromatic absorption. The amine C-N appears at 1291 cm^{-1}. The FT-IR spectrum for compound B1-Br is presented in Figure 7, and summarized in Table 5.

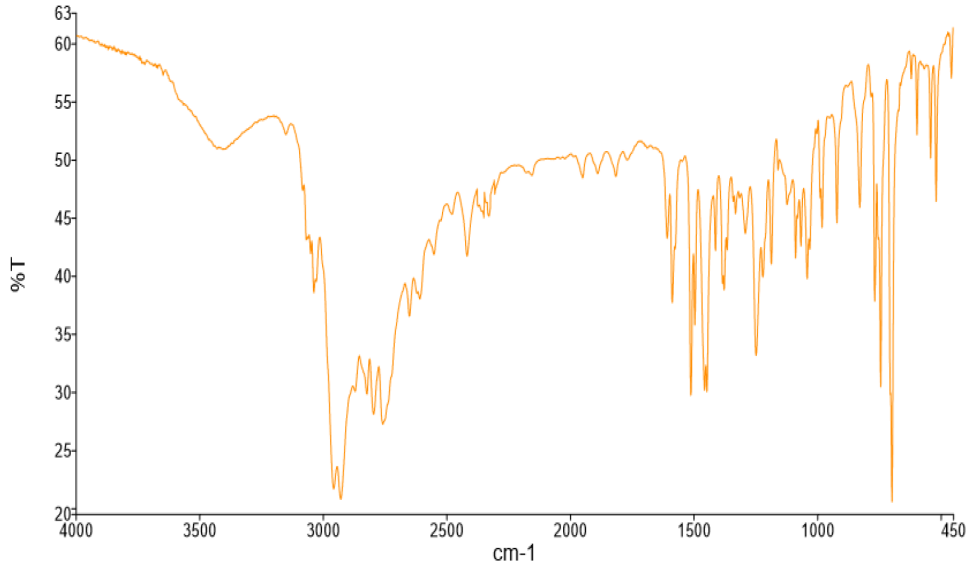
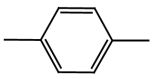
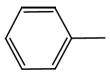


Figure 7. FT-IR spectrum of compound B1-Br (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol).

Table 5. Summary of FT-IR Spectral Data for Compound B1-Br (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol)

Functional group	**Wavenumber (cm^{-1})**	**Intensity**
O-H	3407	Strong
N-C	1291	Weak
C-O-C	1248	Strong
Ar-C=C	1456-1741	Weak, multiple bands, medium
Ar-C-H	3039	Strong
	827	
	750	

FT-IR spectroscopy was employed to determine the functional groups present in compound B1-Cl. The FT-IR spectrum is presented in Figure 8 and summarized in Table 6. It shows a characteristic absorption band at 3426 cm^{-1} corresponding to O-H stretching vibration. The peaks at 1698 and 1465 cm^{-1} are due to bending aromatic C=C. The peak for the N-C stretching appears at 1292 cm^{-1}. The C-O-C bonds appears at 1264 cm^{-1}. The aromatic C-H peak is at 3039 cm^{-1}. The monosubstituted benzene absorption appears at 751 cm^{-1}. Also, the peak at 828 cm^{-1} is due to the *para* substituted benzene absorption.

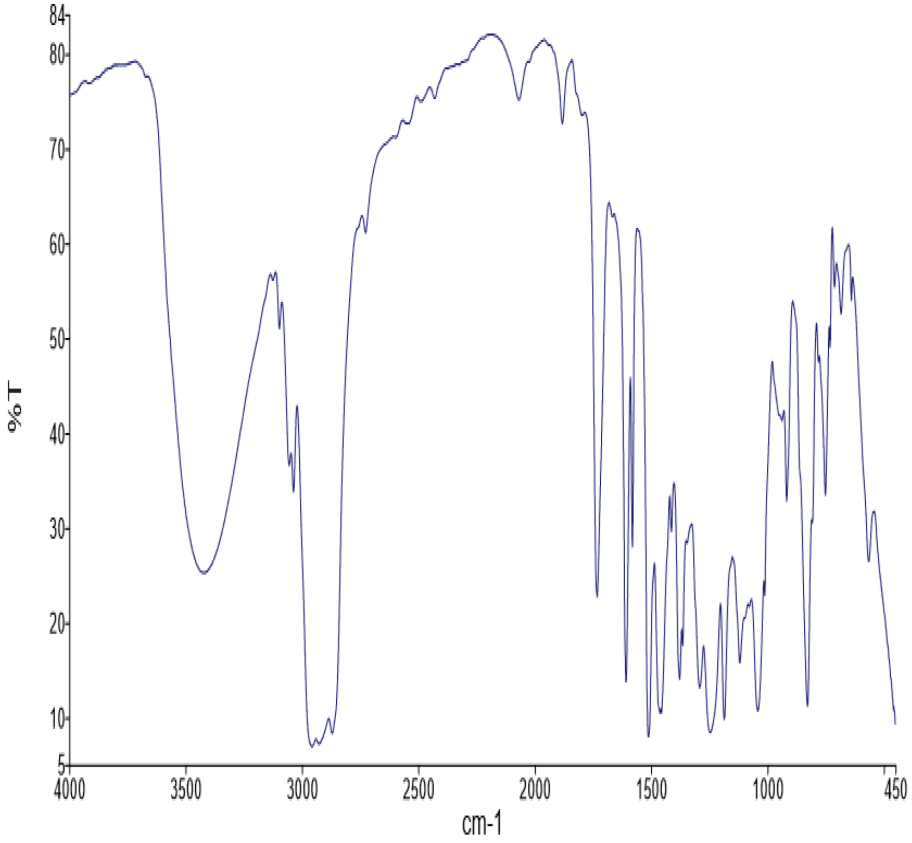


Figure 8. FT-IR spectrum of compound B1-Cl (1-(4-nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol).

Table 6. Summary of FT-IR Spectral Data for Compound B1-Cl (1-(4-Nonylphenoxy)-3-(*cis*-2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
O-H	3426	Strong
N-C	1292	Weak
C-O-C	1264	Strong
Ar-C=C	1456-1698	Weak, multiple bands, Strong
Ar-C-H	3039	Strong
Ar- *para*	828	Weak
Ar-mono	751	Medium

3.2.2 Characterization of Compounds A2, B2-Br, and B2-Cl

^{1}H NMR spectra analysis confirm the structure of compounds A2, B2- Br, and B2-Cl. The proton NMR spectrum of compound A2 is displayed in Figure 9 and the peak assignments are presented in Table 7. The chemical shifts of the three aromatic rings appear between 6.90 and 7.25 ppm. The spectrum shows the long alkyl chain (C_9H_{19}) chemical shifts in the 0.96 and 2.55 ppm region. The methylene proton between nitrogen atom and carbon attached to O-H appears at 2.62 ppm.

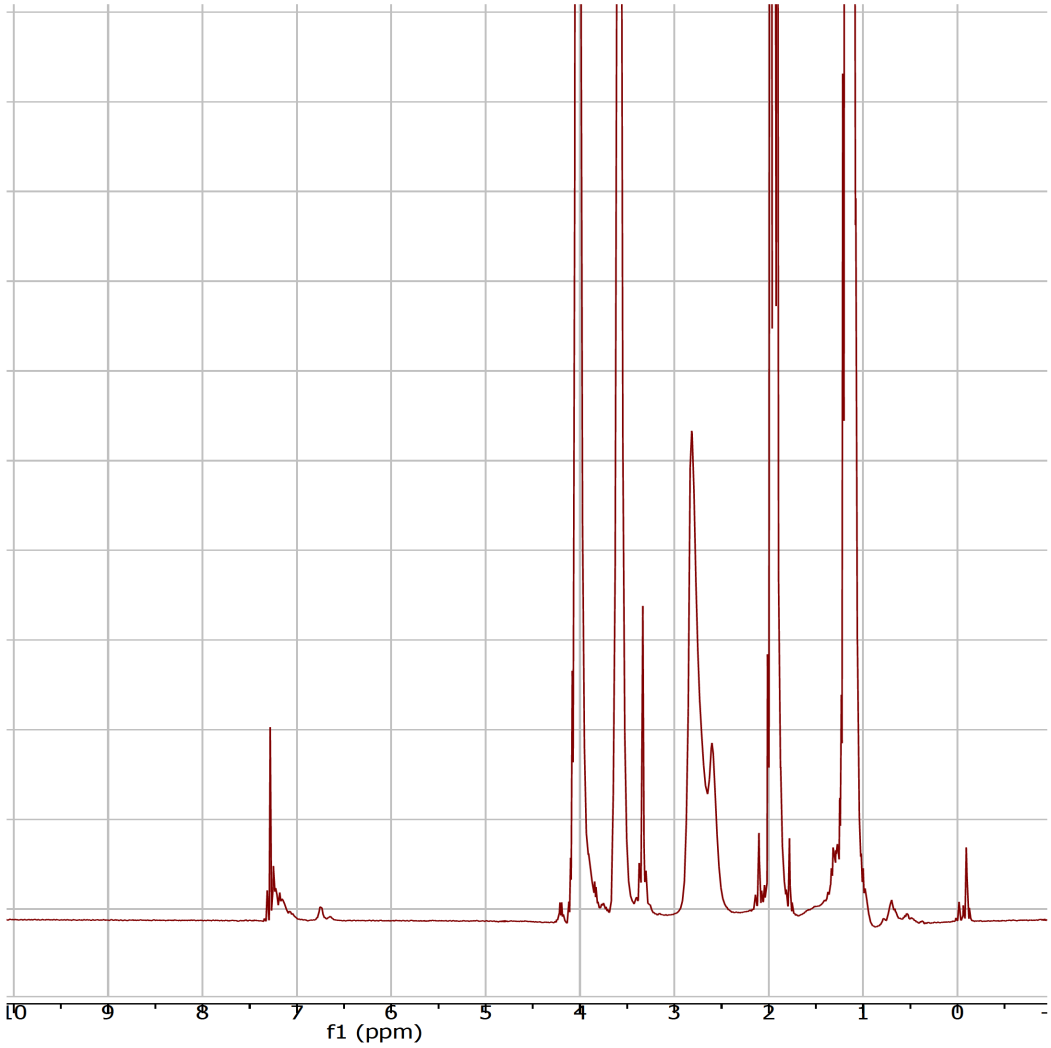
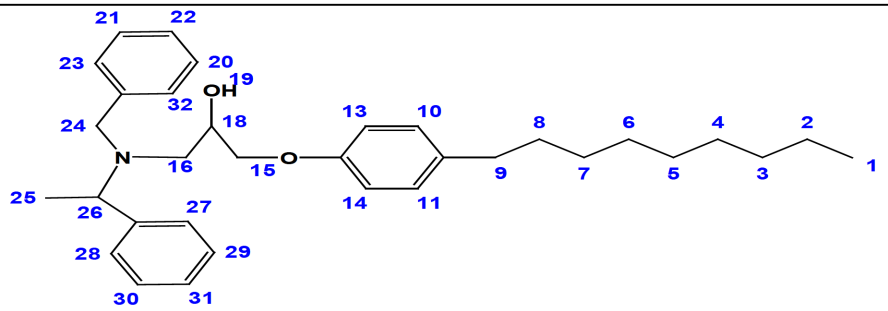
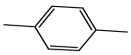
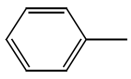
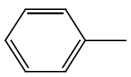


Figure 9. 400 MHz ^{1}H NMR spectrum of compound A2 (1-(4-nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol) in $CDCl_3$.

Table 7. Observed ^{1}H NMR Chemical Shifts for Compound A2 (1-(4-Nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol)



Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
	10, 11	7.01	*para*-Aromatic
	13, 14	6.72	rings
CH	18, 26	3.96, 4.08	
CH_2	15	4.22, 3.97	
	16	2.63, 2.38	
	24	3.62, 3.70	
OH	17	2.62	Alcohol
	22	7.07	Mono-aromatic
	21, 20	7.14	rings
	23, 32	7.06	
	27, 28	7.12	Mono-aromatic
	29, 30	7.21	rings
	31	7.08	
CH_3	25	1.38	

The proton NMR spectrum of compound B2-Br is displayed in Figure 10 and the peak assignments are presented in Table 8. The chemical shifts of the four aromatic rings appear between 6.72 and 7.14 ppm. The spectrum shows the long alkyl chain (C_9H_{19}) chemical shifts between 0.96 - 2.55 ppm. The methylene proton attached to the carbon next to the aromatic ring and nitrogen atom appears at 4.50 ppm. The hydrogen of the hydroxide group appears at 1.90 ppm.

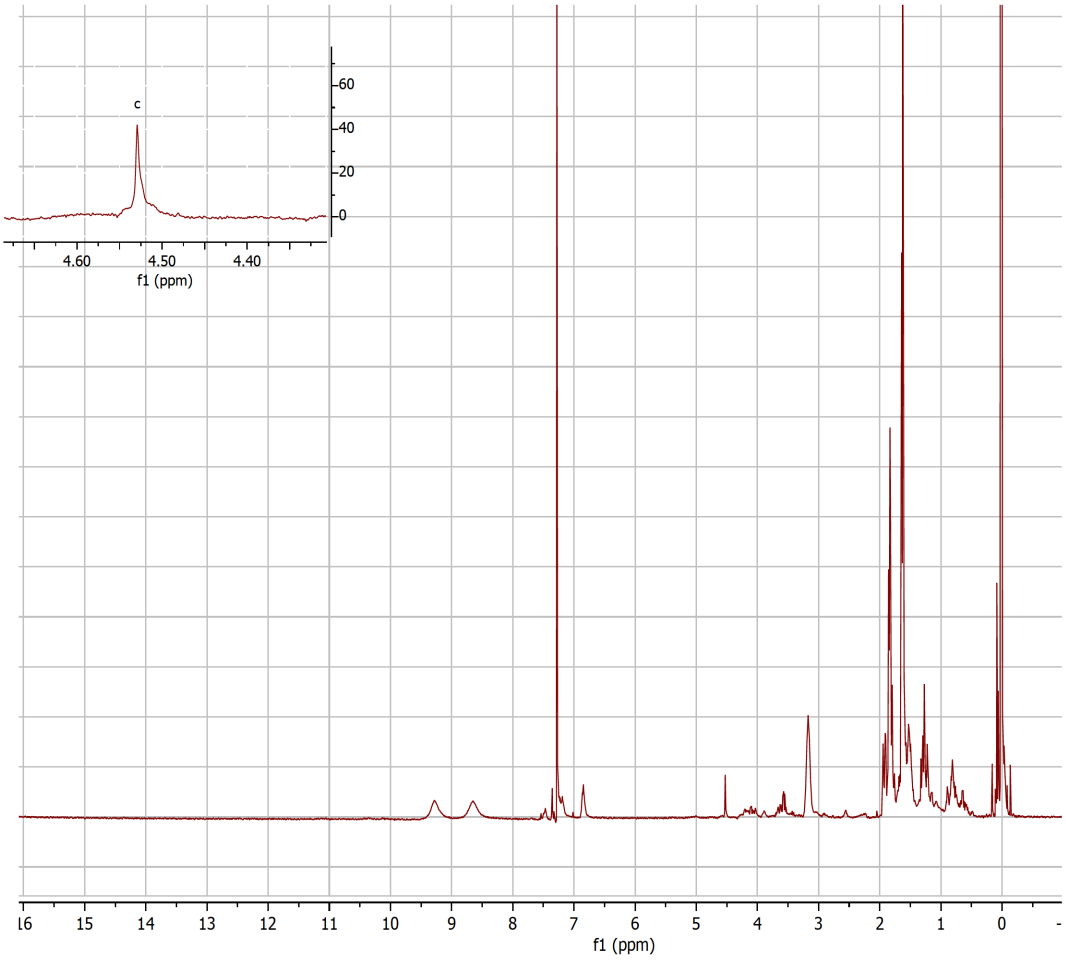
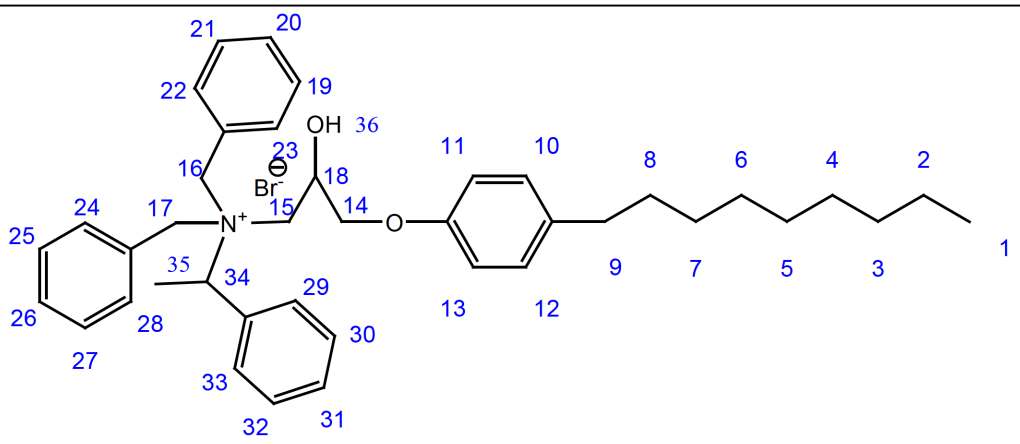
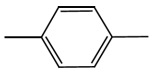
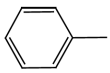


Figure 10. 400 MHz ^{1}H NMR spectrum of compound B2-Br (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol) in $CDCl_3$.

Table 8. Observed ^{1}H NMR Chemical Shifts for Compound B2-Br (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol)



Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
OH	36	1.90	Alcohol
	19, 23	7.06	*para*-Aromatic rings
	24, 28	7.07	
	29, 33	7.14	
	10, 12	7.01	Mono-aromatic rings
	11, 13	6.72	
CH_3	35	1.36	

The ^{1}H NMR spectrum of compound B2-Cl is displayed in Figure11, in and the peak assignments are presented in Table 9. The chemical shifts of the four aromatic rings appear between 6.72 and 7.14 ppm. The spectrum shows the long alkyl chain (C_9H_{19}) chemical shifts at 0.96 - 2.55 ppm. The methylene group attached to the nitrogen atom appears at 4.63 ppm. The hydrogen of the hydroxide group appears at 2.54 ppm.

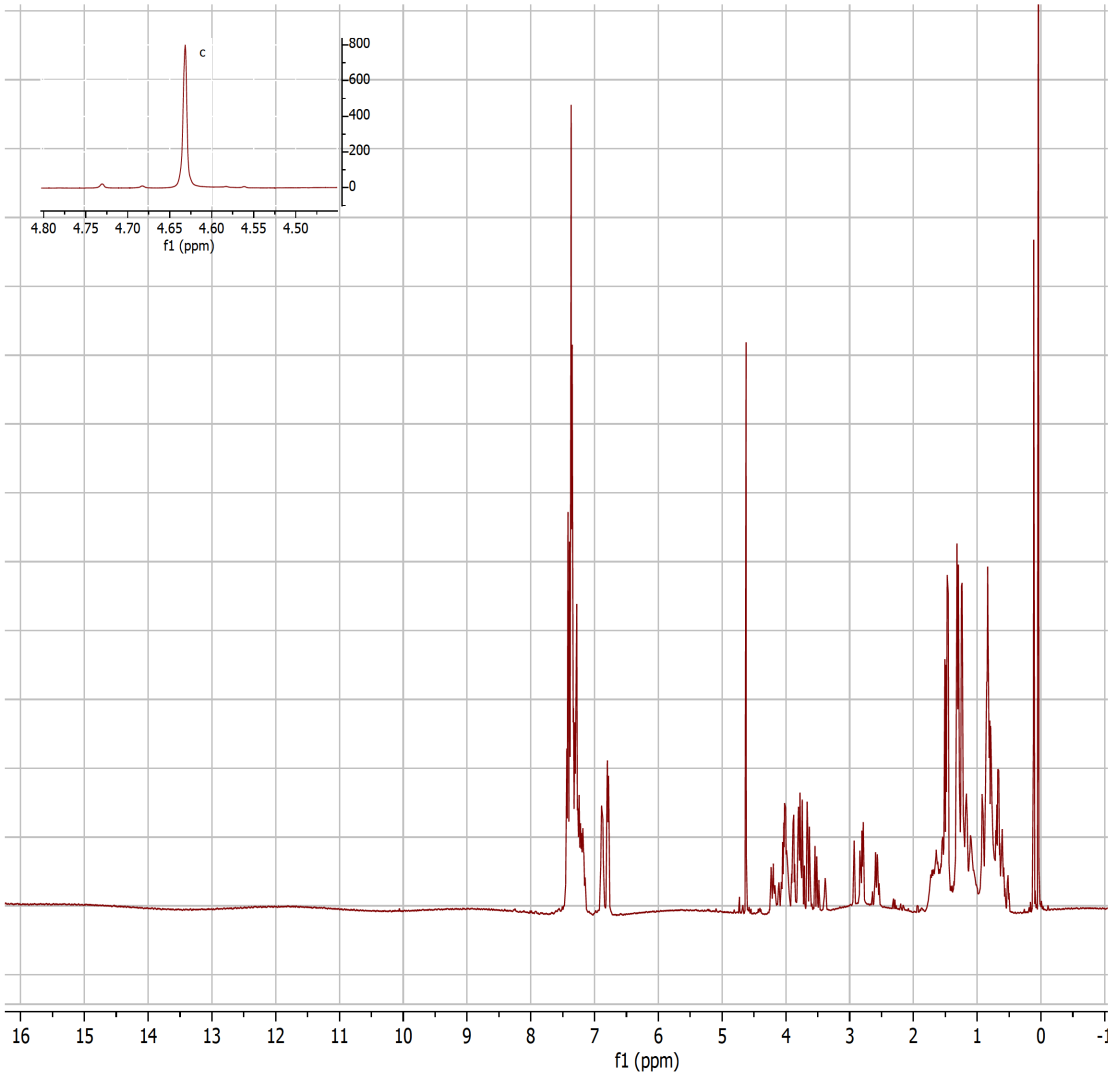
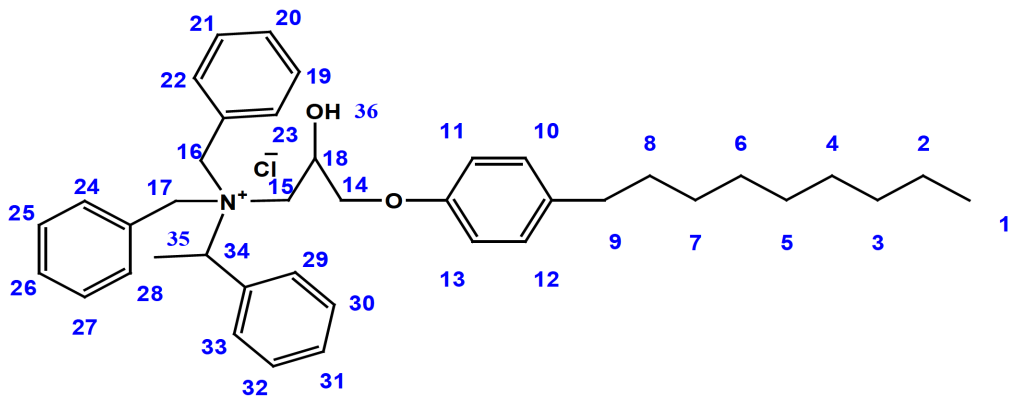


Figure 11. 400 MHz ^{1}H NMR spectra of compound B2-Cl (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol) in $CDCl_3$.

Table 9. Observed ^{1}H NMR Chemical Shifts for Compound B2-Cl (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol)



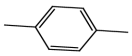
Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
	19, 23	7.06	*Para*-Aromatic rings
	24, 28	7.07	
	29, 33	7.14	
	10, 12	7.01	Mono-aromatic rings
	11, 13	6.72	
CH_3	36	1.36	

Figure 12 shows the comparison between the ^{1}H NMR spectra of compounds A2 and B2-X (X=Cl, Br). In the ^{1}H NMR spectrum of compound A2 the peak at 4.22 ppm corresponds to methine attached to the aromatic ring and linked to the nitrogen atom.

Chemical shifts 2.63 and 2.38ppm corresponds to methylene proton attached to nitrogen atom. The peak at 3.63 ppm corresponds to methylene attached to nitrogen atom next to aromatic ring. The spectrum shows chemical shifts evident for the protons located adjacent to the quaternary nitrogen atom for compound B2-X at approximately 4.50 ppm corresponding to methylene attached to the two aromatic rings group linked to the nitrogen atom; 4.55 ppm corresponding to methine proton attached to nitrogen atom and methyl group to linked aromatic ring.

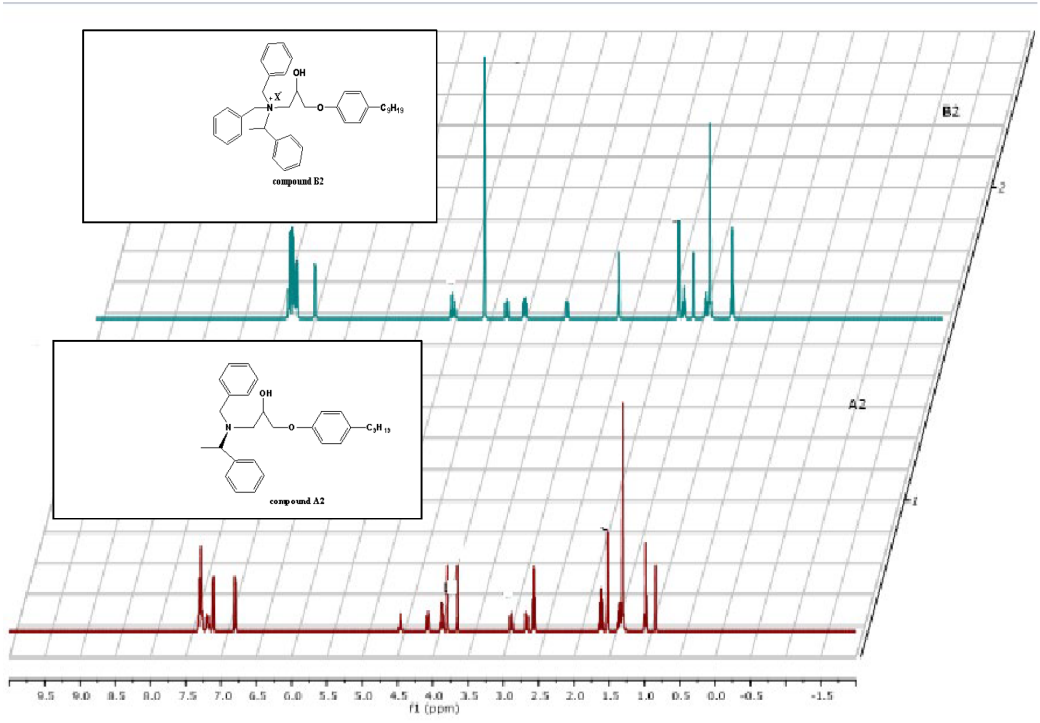


Figure 12. Simulation spectra ^{1}H NMR spectra of compound A2 and B2-X (X= Br, Cl).

The FT-IR absorption peaks are consistent with the functional groups of compound A2. The broad OH stretching vibration absorption appears at 3444 cm^{-1}. The aromatic C-H stretch appears at 2978 cm^{-1}, and the absorption of the C-N shows a sharp band at 1300 cm^{-1}. The peaks at 1745 and 1447 cm^{-1} are due to aromatic C=C bending. The C-O-C band appears at 1246 cm^{-1}. The peak at 874 cm^{-1} is due to *para* substituted aromatic absorption. The FT-IR spectrum for compound A2 is presented in Figure 13 and summarized in Table 10.

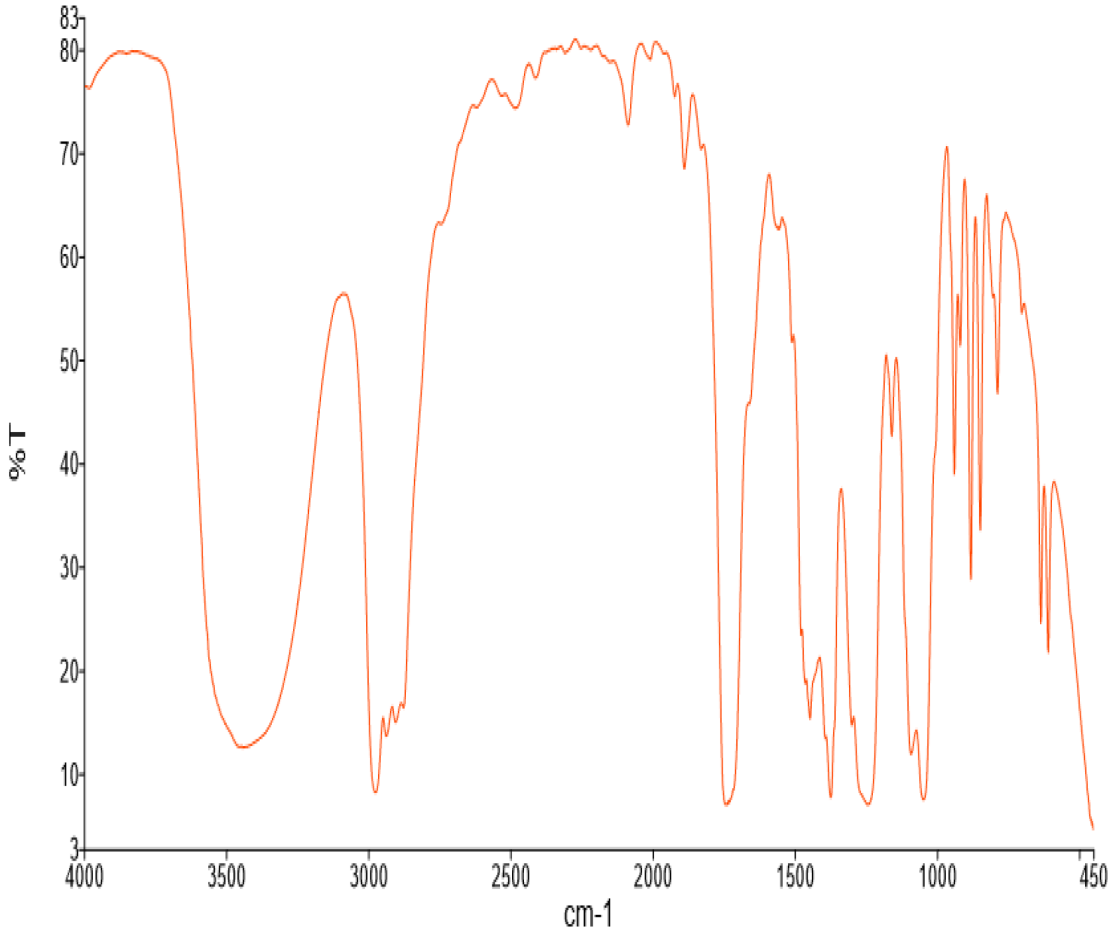


Figure 13. FT-IR spectrum of compound A2 (1-(4-Nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol).

Table 10. Summary of FT-IR Spectral Data for Compound A2 (1-(4-Nonylphenoxy)-3-(N-benzyl-N-((S)-1-phenylethyl)amino)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
O-H	3444	Strong
N-C	1300	Weak
C-O-C	1246	Strong
Ar-C=C	1447, 1745	Weak, multiple bands, Strong
Ar-C-H	2978	Strong
Ar-*para*	847	

The FT-IR absorption peaks are consistent with the functional groups of compound B2-Br. The FT-IR spectrum of compound B2-Br is presented in Figure 14 summarized in Table 11. The broad OH stretching vibration absorption appears as broad peak at 3437 cm^{-1}. Aromatic C-H stretch appeared at 3028 cm^{-1}. The peaks at 1741 and 1511 cm^{-1} are due to aromatic C=C bending. The C-O-C band appears at 1186 cm^{-1}. The peak at 716 cm^{-1} is due to the monosubstituted aromatic absorption, the peak at 827 cm^{-1} is due to the *para* substituted aromatic absorption. The amine C-N absorption appears at 1247 cm^{-1}.

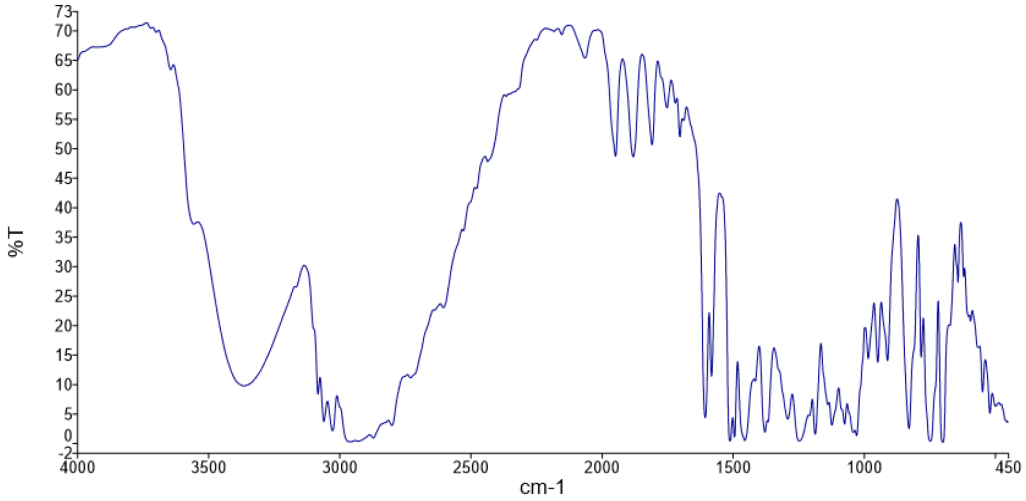
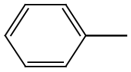
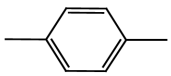


Figure 14. FT-IR spectrum of compound B2-Br (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol).

Table 11. Summary of FT-IR Spectral Data for Compound B2-Br (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium bromo)propan-2-ol)

Functional group	**Wavenumber (cm^{-1})**	**Intensity**
OH	3437	Strong
N-C	1247	Weak
Ar-C=C	1741, 1511	Weak, multiple bands, medium
C-H (Aromatic)	3028	Strong
	746	
	827	
C-O-C	1186	Strong

The FT-IR absorption peaks are consistent with the functional groups of compound B2-Cl. The OH stretching vibration absorption appears as a broad peak at 3437 cm^{-1}. The aromatic C-H stretch appears at 2966 cm^{-1}. The peaks at 1695 and 1511 cm^{-1} are due to the aromatic C=C bending. The C-O-C band appears at 1186 cm^{-1}. The peak at 749 cm^{-1} is due to monosubstituted aromatic absorption. The FT-IR spectrum of compound B2-Cl is presented in Figure 15 and summarized Table 12.

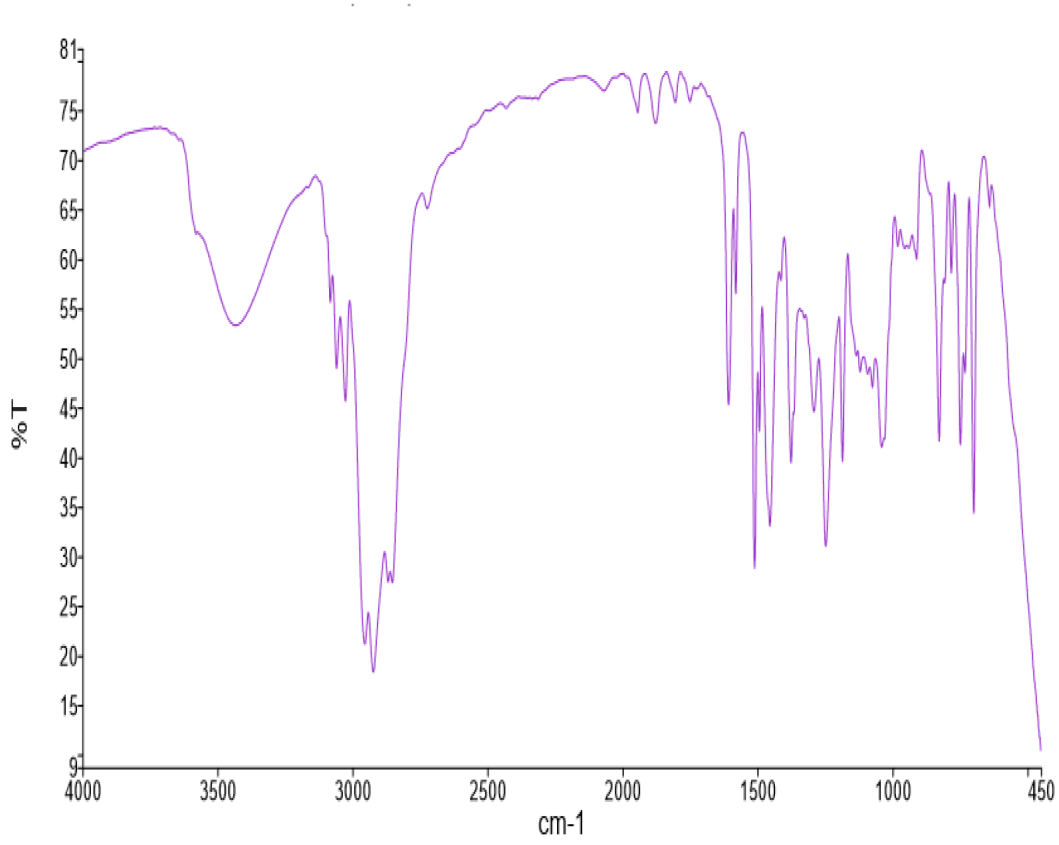
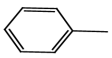
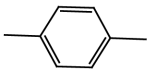


Figure 15. FT-IR spectrum of compound B2-Cl (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol).

Table 12. Summary of FT-IR Spectral Data for Compound B2-Cl (1-(4-Nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammonium chloro)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
OH	3437	Strong
N-C	1247	Weak
Ar-C=C	1512, 1695	Weak, multiple bands, medium
Ar-C-H	2966	Strong
	749	
	827	
C-O-C	1186	Strong

3.2.3 Characterization of Compounds A3, B3-Br, and B3-Cl

The ^{1}H NMR compound of A3 is displayed in Figure 16, and the peak assignments are presented in Table 13. The chemical shifts of the three aromatic rings appears between the 6.43 and 9.98 ppm region. The spectrum shows the long alkyl chain (C_9H_{19}) chemical shifts between the 0.96 and 2.55 ppm region. The chemical shifts for methylene protons attached to the nitrogen appears at 3.74 ppm.

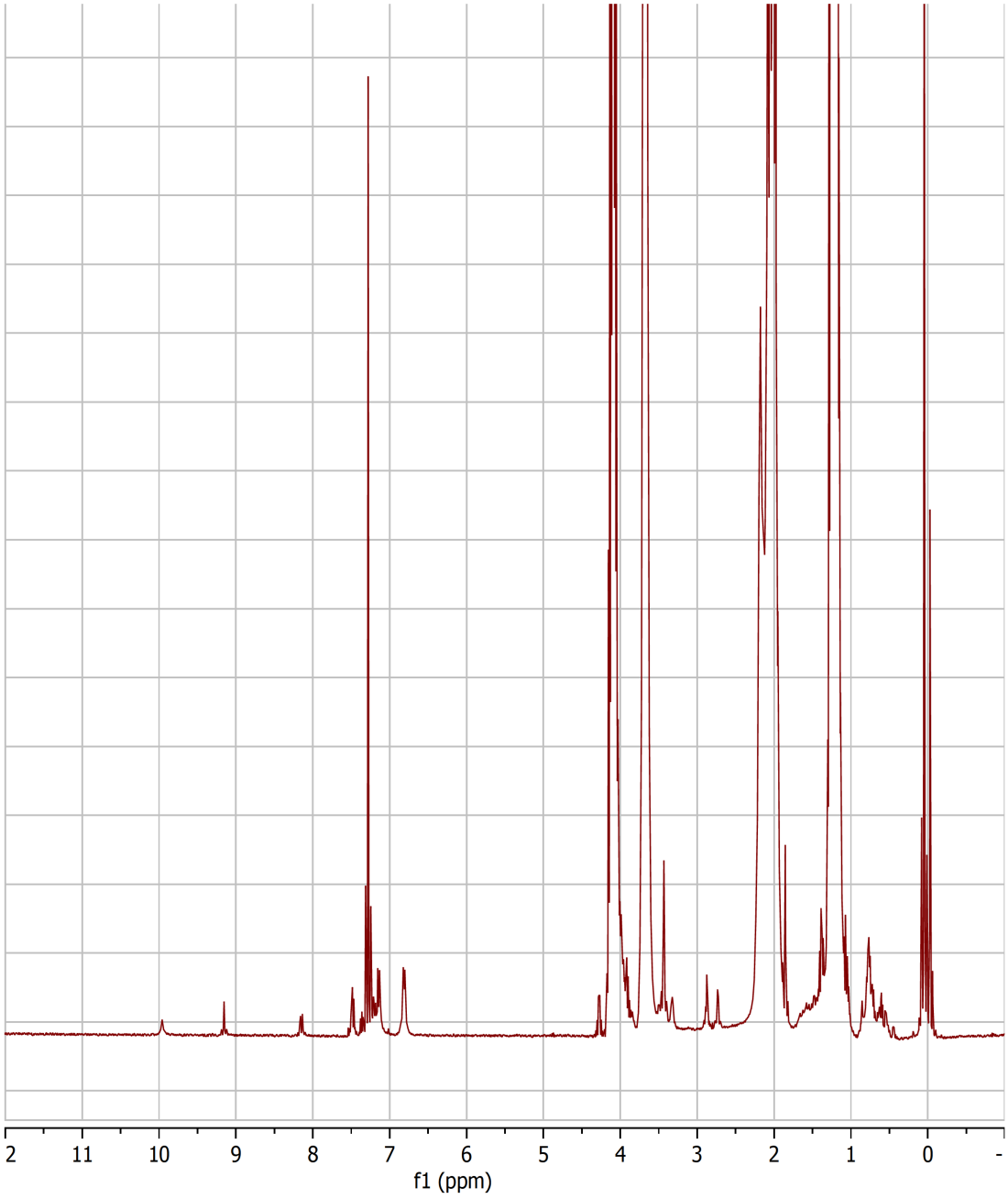
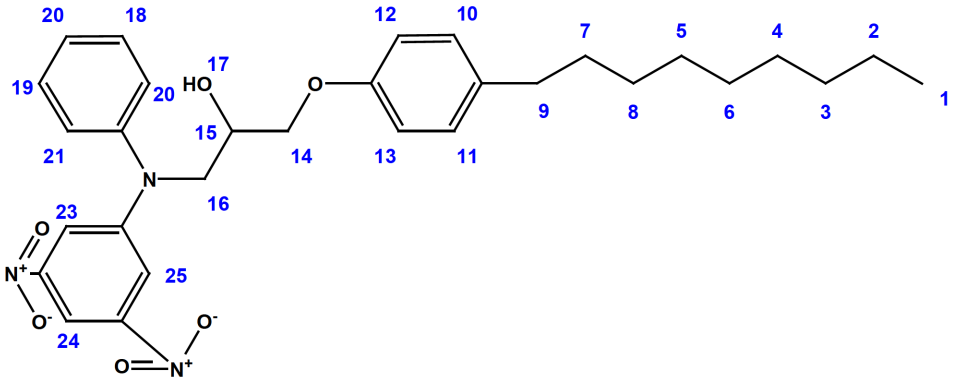
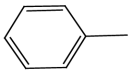
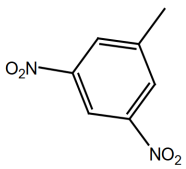


Figure 16. 400 MHz ^{1}H NMR spectrum of compound A3 (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol) in $CDCl_3$.

Table 13. Observed ^{1}H NMR Chemical Shifts for Compound A3 (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol)



Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
OH	17	2.50	Alcohol
	18, 19	7.04	Mono-aromatic rings
	20, 21	6.43	
	22	6.95	
	23, 25	9.27	
	24	9.98	

^{1}H NMR spectrum confirms the structure of compound B3-Br. The ^{1}H NMR spectrum of compound B3 is displayed in Figure 17, and the peak assignments are presented in Table 14. The chemical shifts of the four aromatic rings appear between 6.72 and 7.82 ppm. The spectrum shows the long alkyl chain (C_9H_{19}) chemical shifts between 0.96 and 2.55 ppm. The chemical shifts for methylene protons attached to the nitrogen atom appear 4.63 ppm. The hydrogen of the hydroxide group appears at 2.50 ppm.

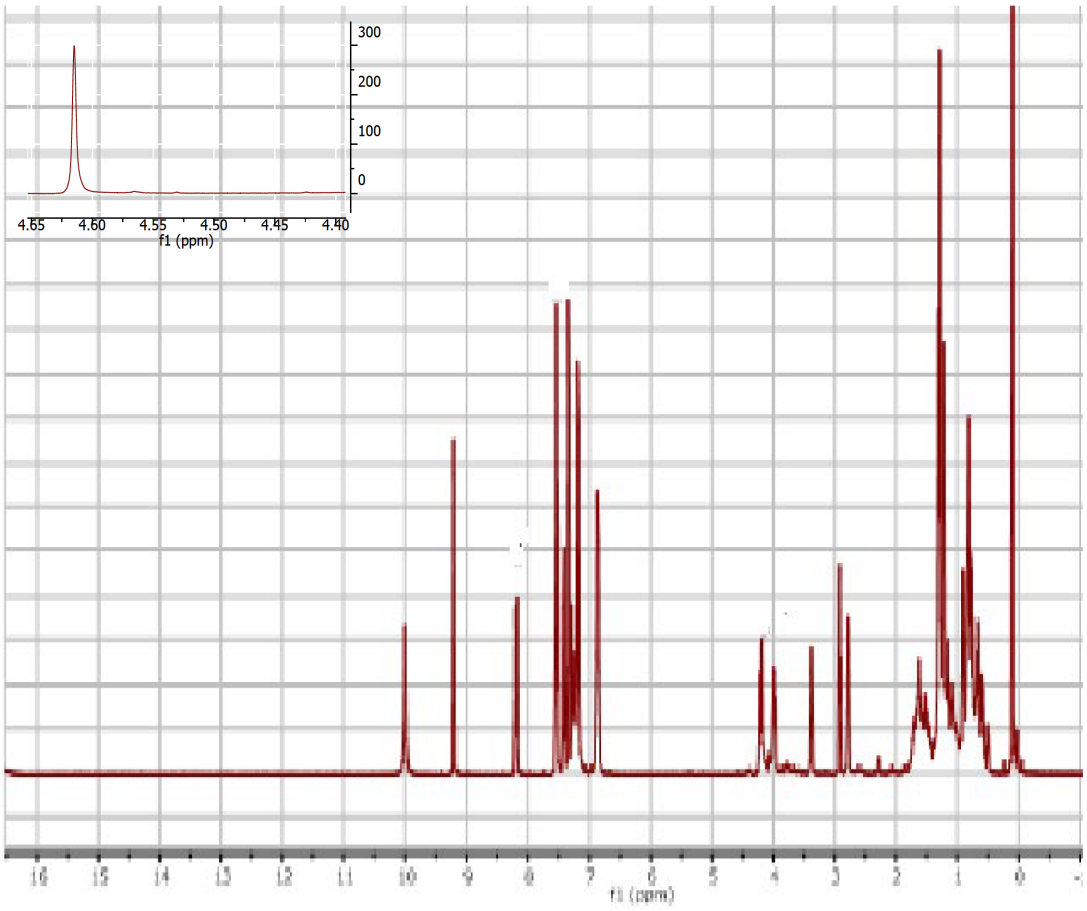
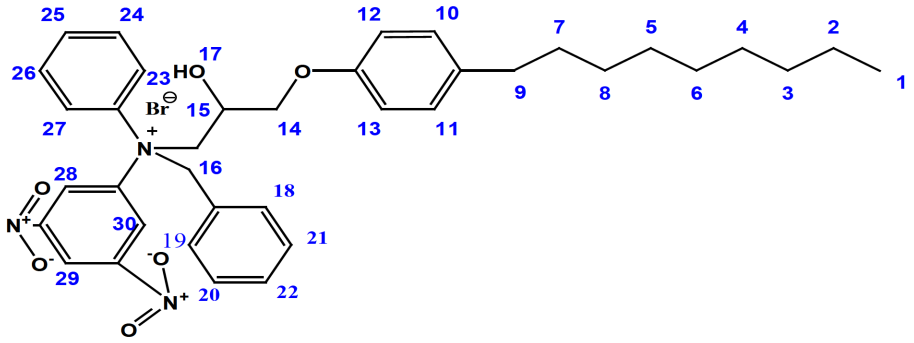
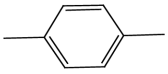
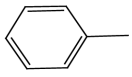
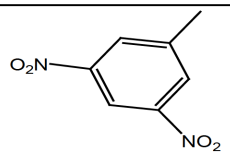


Figure 17. 400 MHz ^{1}H NMR spectrum of compound B3-Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol) in $CDCl_3$.

Table 14. Observed ^{1}H NMR Chemical Shifts for Compound B3-Br (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol)



Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
OH	14	2.50	Alcohol
	18, 19	7.06	*para*-Aromatic
	20, 21	7.07	rings
	22, 23	7.14	Double
	24, 25	7.82	
	26, 27	7.56	
	10, 11	7.01	Mono-aromatic
	12, 13	6.72	rings

	23, 25	9.27	Singlet
	24	9.98	

The ^{1}H NMR spectrum confirms the structure of compound B3-Cl. The ^{1}H NMR spectrum of compound B3 is displayed in Figure 18, and the peak assignments are presented in Table 15. The chemical shifts of the four aromatic rings appear between 6.72 and 7.82 ppm. The spectrum showed the long alkyl chain (C_9H_{19}) chemical shifts between 0.96 and 2.55 ppm. The chemical shifts for methylene proton attached nitrogen atom appears of 4.53 ppm. The hydrogen hydroxide group appeared at 2.40 ppm.

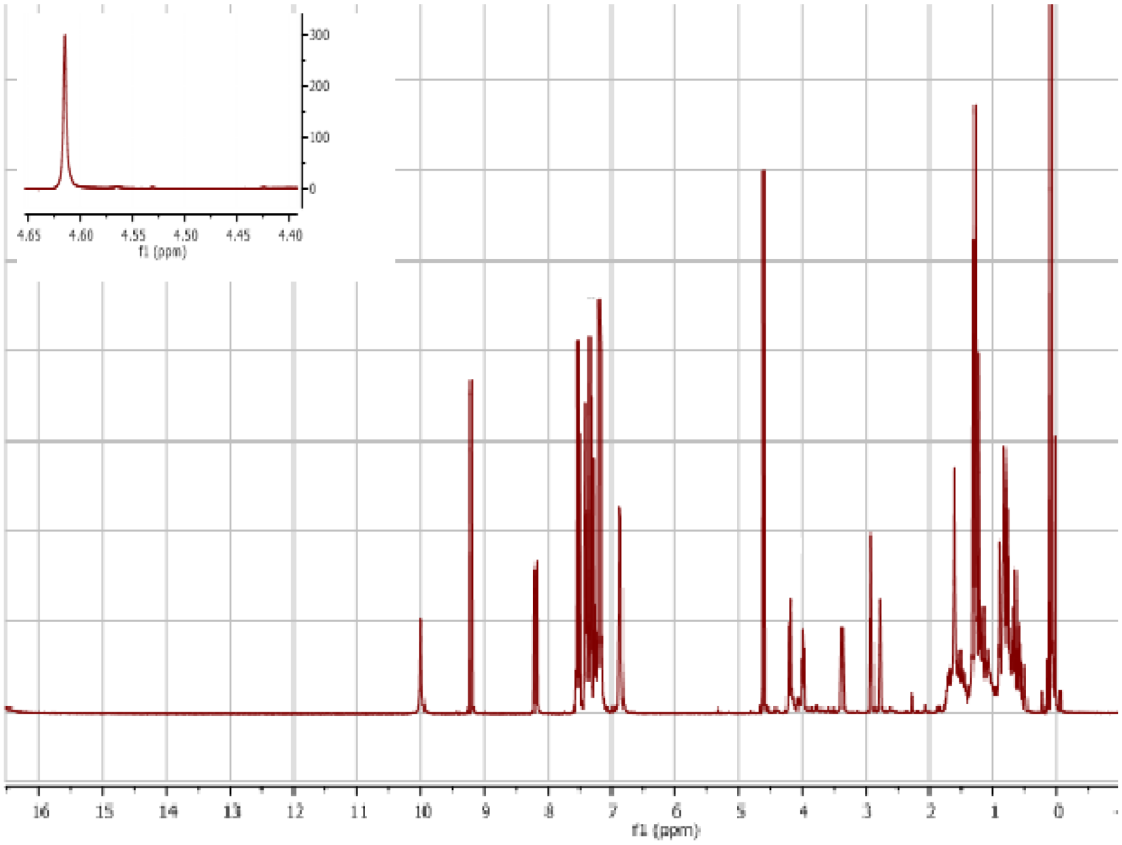
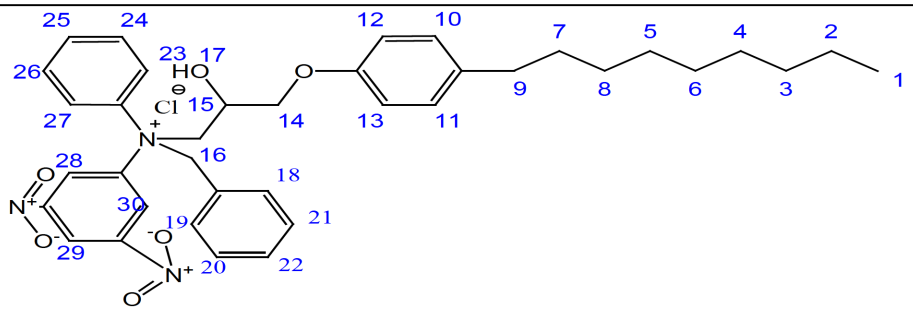


Figure 18. 400 MHz ^{1}H NMR spectrum of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol) in $CDCl_3$.

Table 15. Observed ^{1}H NMR Chemical Shifts for Compound B3-Cl (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol)



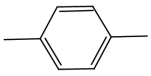
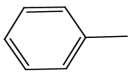
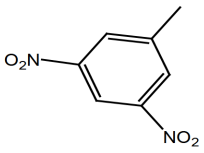
Structure	Proton number	Chemical shift (ppm)	Remark
C_9H_{19}	1-9	0.96, 2.55	Alkyl chain
OH	17	2.40	Alcohol
	18, 19	7.06	*para*-Aromatic rings
	20, 21	7.07	
	22, 23	7.14	
	24, 25	7.82	
	26, 27	7.56	
	10, 11	7.01	Mono-aromatic rings
	12, 13	6.72	
	23, 25	9.27	Singlet
	24	9.98	

Figure 19 shows the comparisons between the ^{1}H NMR spectra of compounds A3 and B3-X (X=Cl, Br). In the ^{1}H NMR spectrum of compound A3 the peak at 4.29 ppm corresponds to methylene protons attached to the nitrogen and methine attached to O-H group, 7.82 ppm corresponds protons adjacent to carbon (aromatic) attached to tertiary nitrogen atom. The peak at 7.56 ppm corresponds the aromatic protons carbon adjacent to the carbon attached to the NO_2 groups. The chemical shift at 9.27 ppm corresponds to the proton (aromatic) attached to the carbon between the NO_2 groups. The spectrum shows chemical shifts evident of the protons located adjacent to the quaternary nitrogen atom for compound B3-X, 4.29. The peak at 4.29 ppm corresponds to methylene protons attached to the nitrogen and methine attached to O-H group, 7.82 ppm corresponds protons adjacent to carbon (aromatic) attached to tertiary nitrogen atom. The peak at 7.56 ppm corresponds to the aromatic protons of the carbon adjacent to the carbon attached to the NO_2 groups. The chemical shift at 9.27 ppm corresponds attached to the proton (aromatic) to the carbon between the NO_2 groups. Addition of the benzyl groups results in peaks appearing at 4.63 and 4.462 ppm due to the methylene groups of the bromo and chloro salts, respectively.

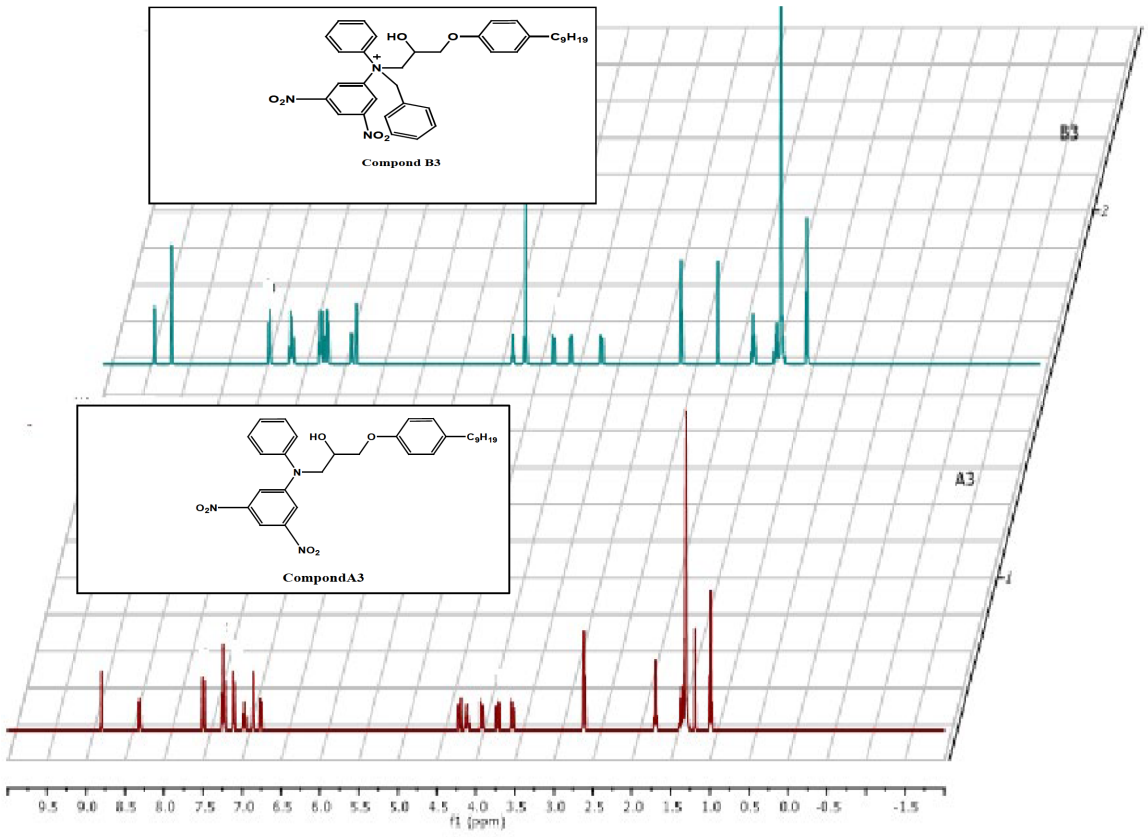


Figure 19. Simulation ^{1}H NMR spectra of compounds A3 and B3-X (X= Br, Cl).

FT-IR absorption peaks are consistent with the functional groups of compounds A3. The OH stretching vibration absorption appears at 3335 cm^{-1}. The aromatic C-H stretch appears at 2974 cm^{-1}, and the C-N appears a sharp band at 1090 cm^{-1}. The peaks at 1741 and 1455 cm^{-1} are due to aromatic C=C bending. The C-O-C bonds appear at 1050 cm^{-1}. The peak at 881 cm^{-1} is due to *para* substituted aromatic absorption. The FT-IR spectrum for compound A3 is presented in Figure 20 and summarized Table 16.

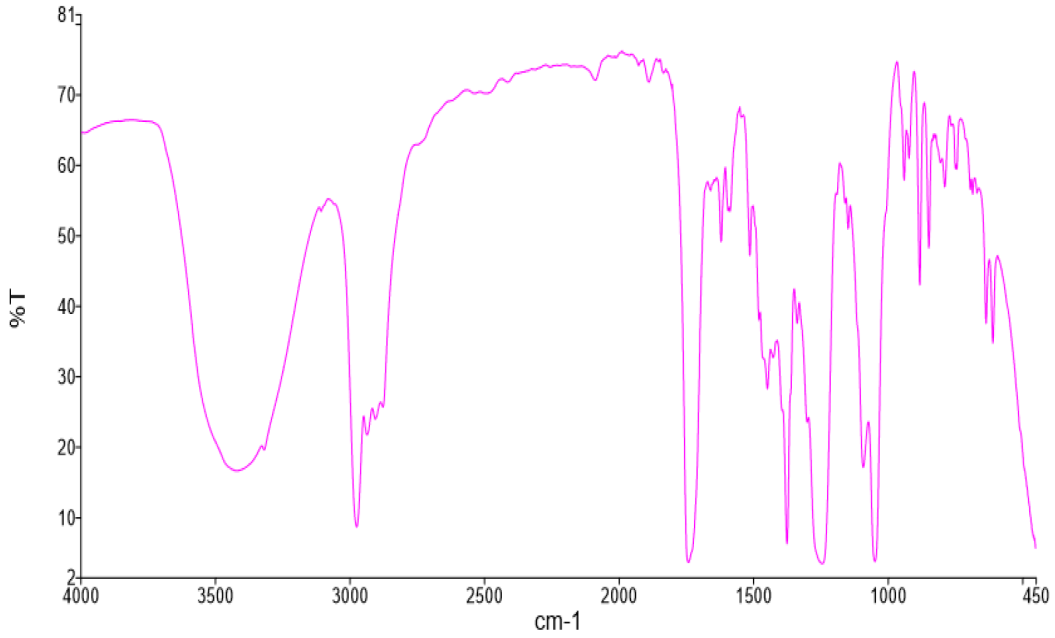


Figure 20. FT-IR spectrum of compound A3 (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol).

Table 16. Summary of FT-IR Spectral Data for Compound A3 (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylamino)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
O-H	3335	Strong
N-C	1090	Weak
C-O-C	1050	Strong
Ar-C=C	1455	Weak, multiple bands
	1741	Strong
Ar-C-H	2974	Strong
Ar-*para*	881	

FT-IR spectroscopy was employed to determine the functional groups and type of bonds present in compound B3-Cl. The FT-IR spectrum of compound B3-Cl is presented in Figure 21 and summarized in Table 17. The OH stretching vibration absorption appears as a broad band 3435 cm^{-1}. The aromatic C-H stretch appears at 2961 cm^{-1}. The peaks at 1583 and 1697 cm^{-1} are due to aromatic C=C bending. The C-O-C bands appear at 1146 cm^{-1}. The peak at 749 cm^{-1} is due to monosubstituted aromatic absorption. Also, the peak at 825 cm^{-1} is due to *para* substituted aromatic absorption. The peaks at 1518 and 1337 cm^{-1} are due to NO_2 stretching.

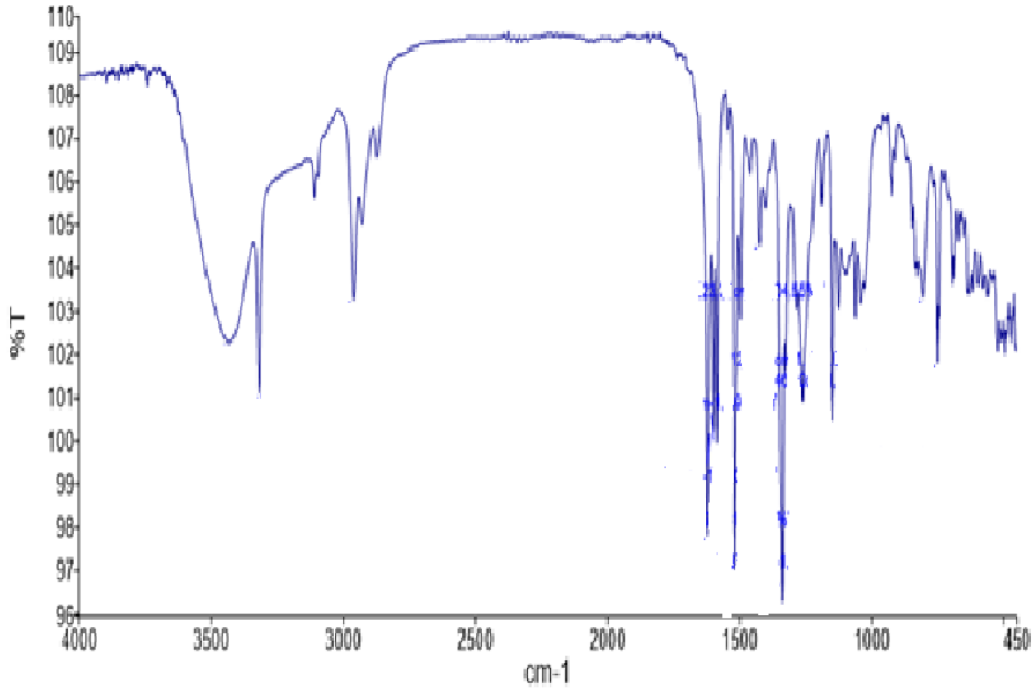
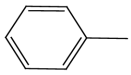
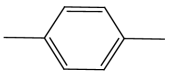


Figure 21. FT-IR spectrum of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol).

Table 17. Summary of FT-IR Spectral Data for Compound B3-Cl (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
O-H	3435	Strong
N-C	1059	Weak
C-O-C	1146	Strong
Ar-C=C	1583, 1697	Weak, multiple bands, Strong
Ar-C-H	2961	Strong
	749	
	825	
NO_2	1518, 1337	Strong

The FT-IR spectroscopy was employed to determine the functional groups and type of bonds present in compound B3-Br. The FT-IR spectrum of compound B3- Br is presented in Figure 22 and summarized in Table18. The OH bond appears as broad absorption at 3317 cm^{-1}. The aromatic C-H stretch appeared at 2853 cm^{-1}. The aromatic C=C appears at 1462 cm^{-1}, and the C-O-C bond appears at 1248 cm^{-1}. The monosubstituted aromatic absorption appears at 692 cm^{-1}. Also, the peak at 825 cm^{-1} is due to the *para* substituted aromatic. The peak at 1377 cm^{-1} is due to C-N absorption.

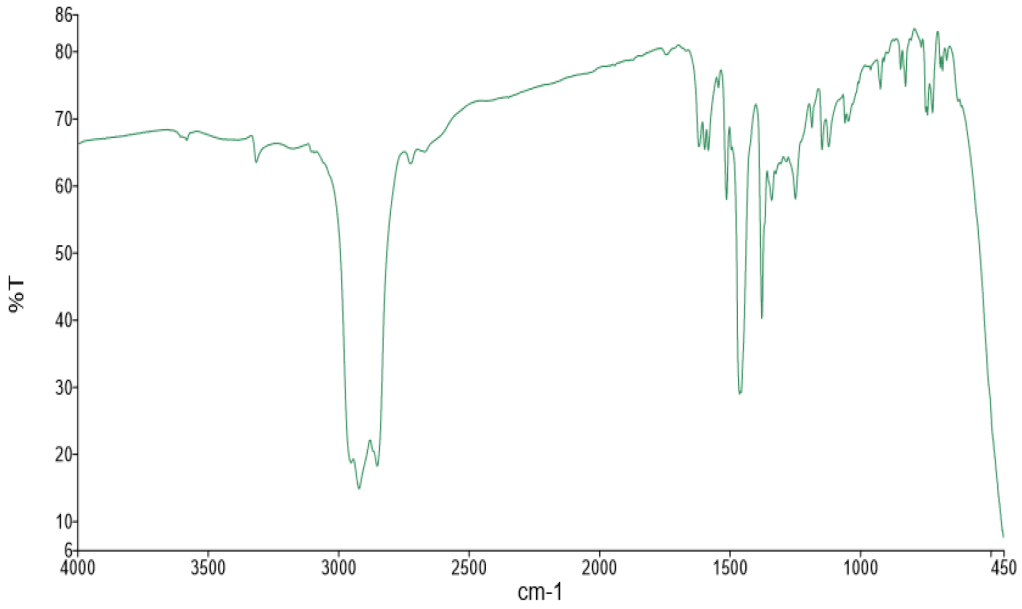
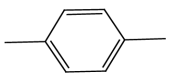
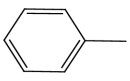


Figure 22. FT-IR spectrum of compound B3-Br (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol).

Table 18. Summary of FT-IR Spectral Data for Compound B3-Br (1-(3-Nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol)

Functional group	Wavenumber (cm^{-1})	Intensity
O-H	3317	Strong
N-C	1377	Weak
C-O-C	1248	Strong
Ar-C=C	1462	Weak, multiple bands
Ar-C-H	2853	Strong
	825	
	692	

Thermal stability was investigated by thermogravimetric analysis (TGA). Compound B3-Cl exhibits an onset of decomposition temperature at 206 °C under nitrogen atmosphere (Figure 23).

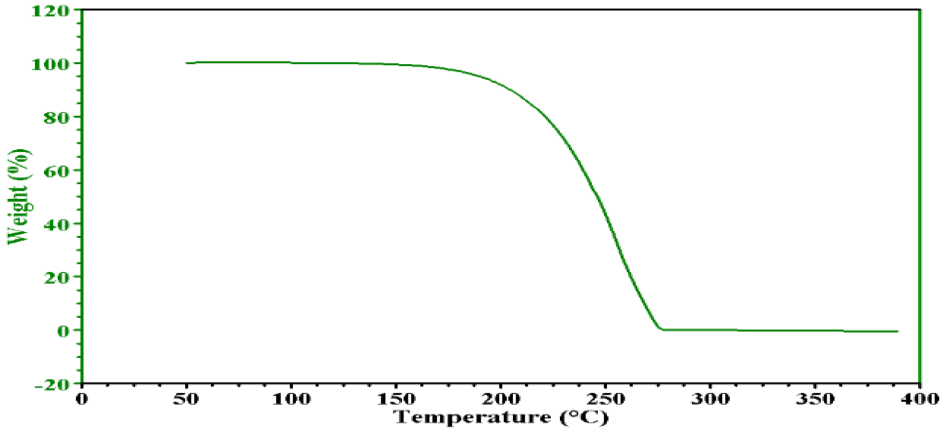


Figure 23. TGA thermogram of compound B3-Cl (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol).

Compound B3-Cl exhibits an onset of decomposition temperature at 207 °C under nitrogen atmosphere (Figure 24). The quaternary benzalkonium salts have similar decomposition temperatures.

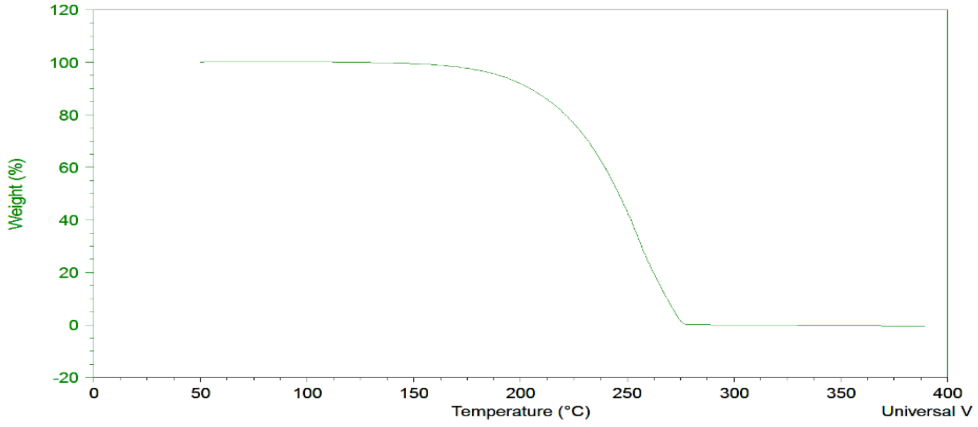


Figure 24. TGA thermogram of compound B3-Br (1-(3-nonylphenoxy)-3-(N-(2, 4-dinitrophenyl)-N-phenyl ammonium bromo)propan-2-ol).

3.3 Thin Layer Chromatography

Thin layer chromatography was used to verify the purity of the B2-Br, B1-Br, B3-Cl, B1-Cl, B2-Cl, and B3 –Br (Figure 25). The TLC plates under UV light show one spot for each compound. These indicate the relative purity of compounds.

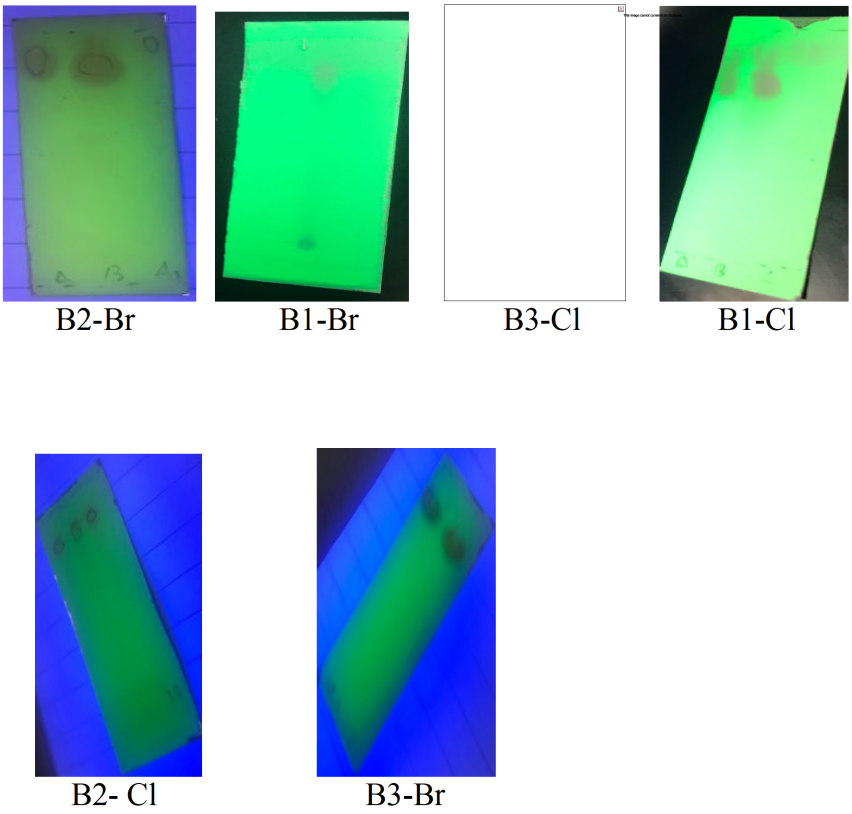
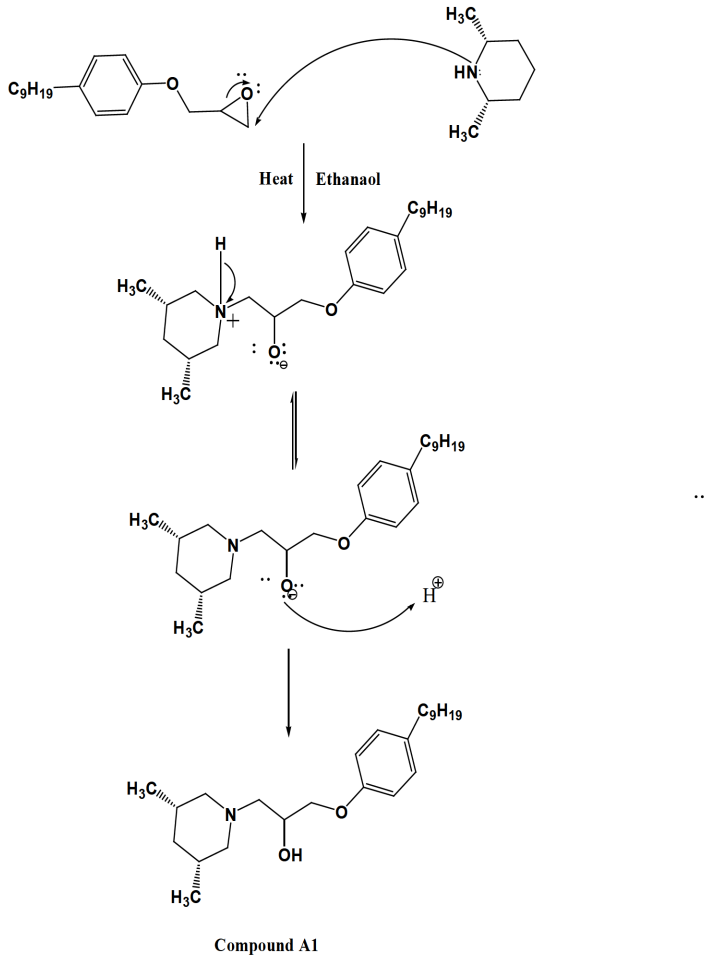


Figure 25. TLC plate under UV light for compounds B2-Br, B1-Br, B3-Cl, B1-Cl, B2-Cl, and B3-Br.

3.4 Reaction Mechanism of Compounds

3.4.1 Mechanism of the Synthesis of Compound A1, by Nucleophilic Addition Reaction

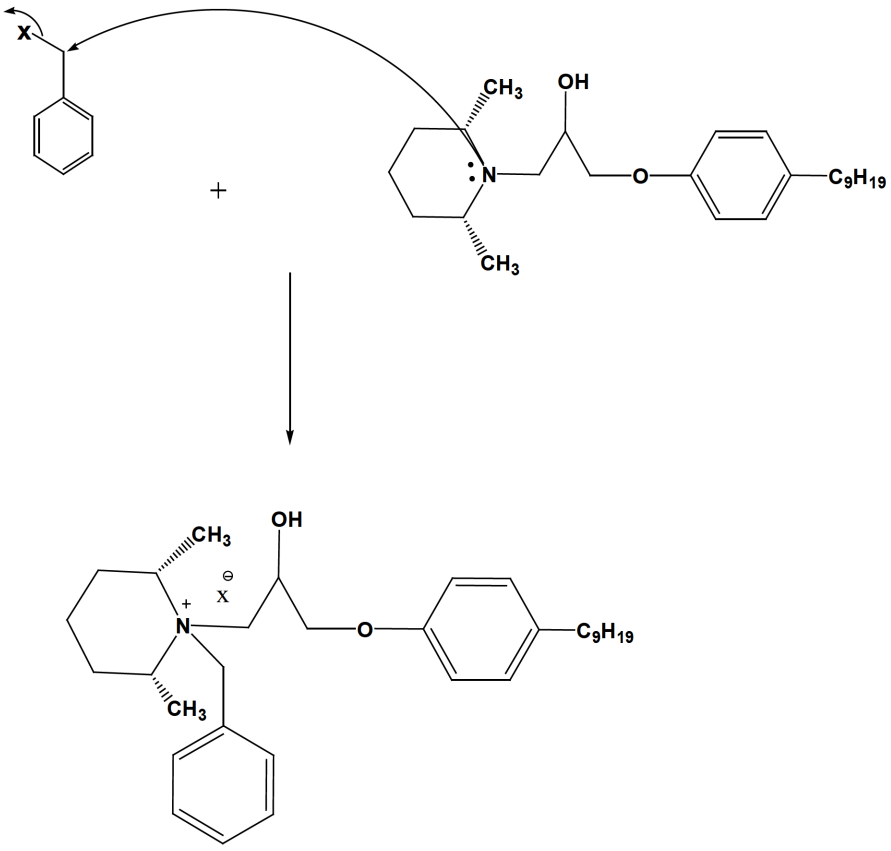
The reactions between the epoxides and the secondary amines are nucleophilic addition reactions. The secondary amine attacks the methylene group of the epoxide resulting in a sequential ring-opening followed by deprotonation and the formation of the tertiary amine. Thereafter, the oxygen anion is protonated to give compound[11] (Scheme 10).



Scheme 10. Mechanism of the synthesis of compound A1, by nucleophilic addition reaction.

3.4.2 Mechanism of the Synthesis of Compound B1, a Bimolecular Substitution Nucleophilic (S_N2) Reaction

In the quaternization reaction, the methylating agent undergoes a nucleophilic attack by the tertiary amine at the methylene group in a nucleophilic substitution (S_N2) reaction via the Menschutkin reaction[12] process (Scheme 11).



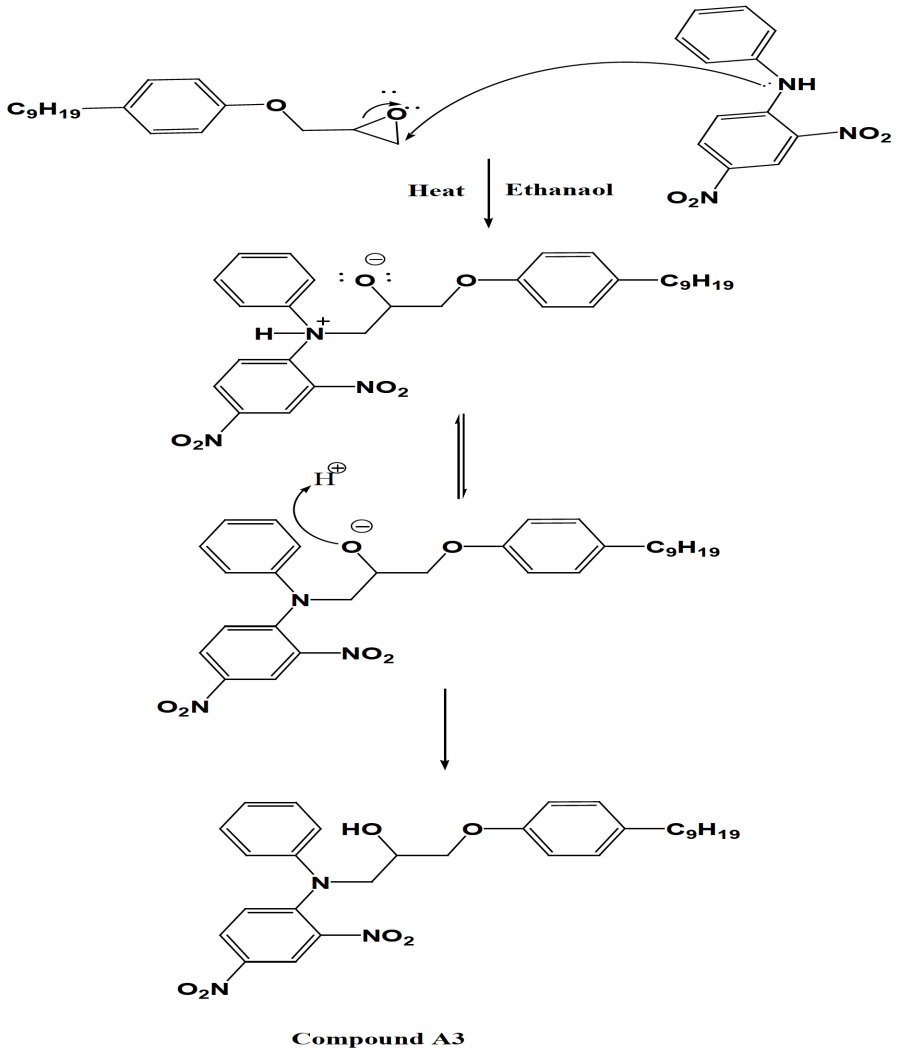
Compound B1

X= Cl, Br

Scheme 11. Mechanism of the synthesis of compounds B1, a bimolecular substitution nucleophilic (S_N2) reaction.

3.4.3 Mechanism of Synthesis of Compound A2, by Nucleophilic Addition Reaction

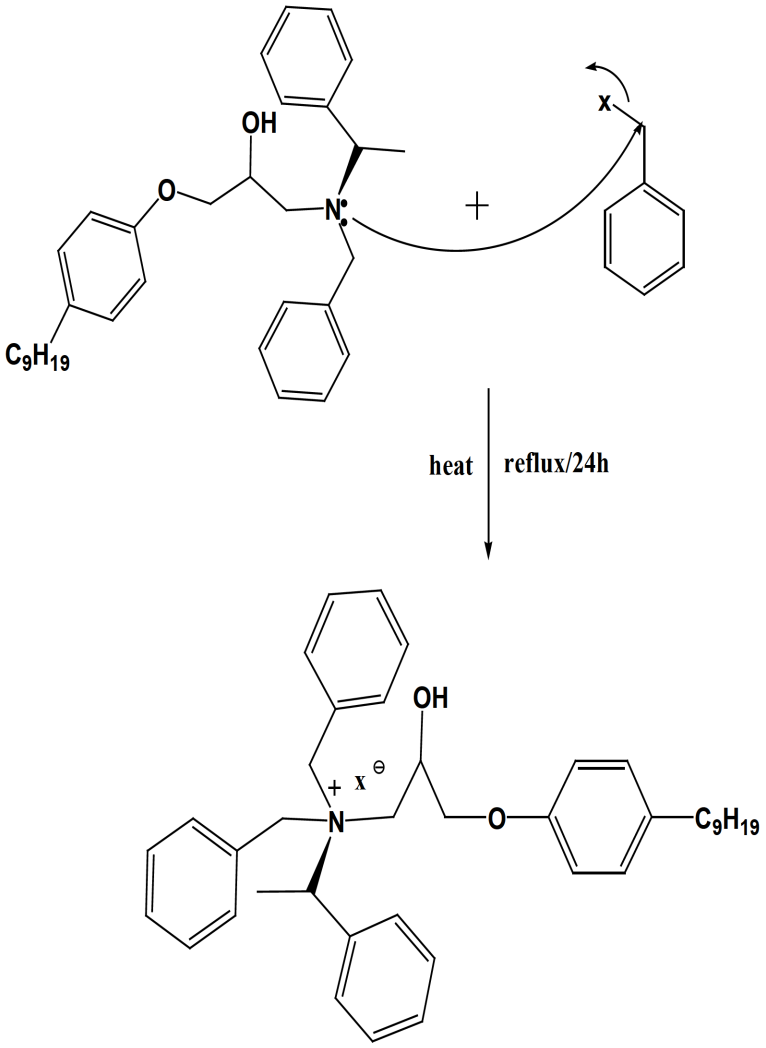
The reactions between the epoxide and secondary amines are nucleophilic addition reaction. The secondary amine attacks the methylene group of the epoxide resulting in a sequential ring-opening followed by deprotonation and the formation of the tertiary amine. Thereafter, the oxygen anion is protonated to give compound[11] (Scheme 12).



Scheme 12. Mechanism of the synthesis of compound A2, by nucleophilic addition reaction.

3.4.4 Mechanism of the Synthesis of Compound B2, a Bimolecular Substitution Nucleophilic (S_N2) Reaction

In the quaternization reaction, the methylating agent undergoes a nucleophilic attack by the tertiary amine at the methylene group in a nucleophilic substitution (S_N2) reaction via the Menschutkin reaction[12] process (Scheme 13).



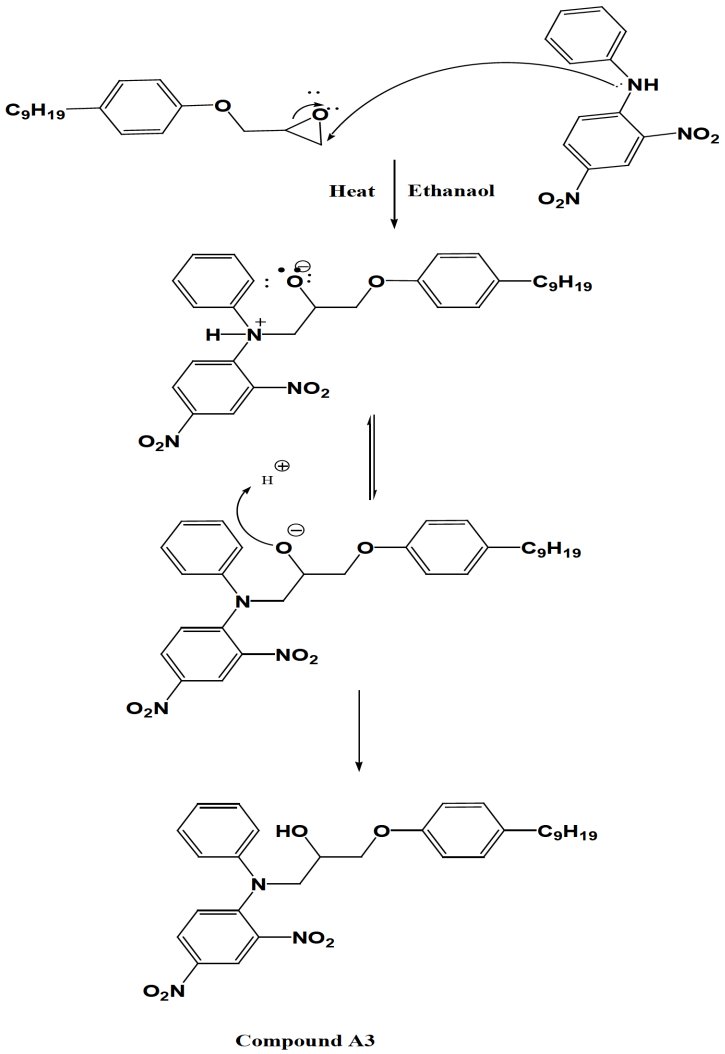
Compound B2

X=Cl, Br

Scheme 13. Mechanism of the synthesis of compound B2, a bimolecular substitution nucleophilic (S_N2) reaction.

3.4.5 Mechanism of Synthesis of Compound A3, by Nucleophilic Addition Reaction

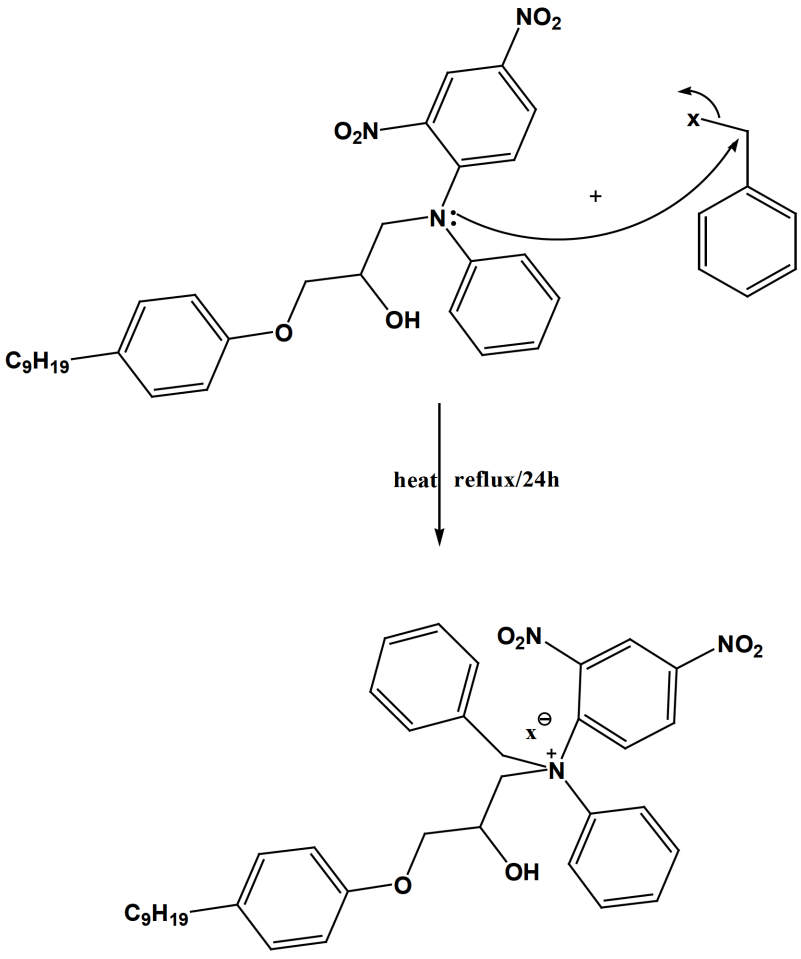
The reactions between the epoxides and the secondary amines are nucleophilic addition reaction. The secondary amine attacks the methylene group of the epoxide resulting in a sequential ring-opening followed by deprotonation and the formation of the tertiary amine. Thereafter, the oxygen anion is protonated to give compound[11] (Scheme 14).



Scheme 14. Mechanism of the synthesis of compound A3, by nucleophilic addition reaction.

3.4.6 Mechanism of the Synthesis of Compound B3, a Bimolecular Substitution Nucleophilic (S_N2) Reaction

In the quaternization reaction, the methylating agent undergoes a nucleophilic attack by the tertiary amine at the methylene group in a nucleophilic substitution (S_N2) reaction via the Menschutkin reaction[12] process (Scheme 15).



Compound B3 X= Cl, Br

Scheme 15. Mechanism of the synthesis of compounds B3, a bimolecular substitution nucleophilic (S_N2) reaction.

CHAPTER IV

CONCLUSION

Bacteria are among the most common infectious agents whose effects can be adverse if the infections are not identified and treated on time. The best approach to address the causative agents is by designing agents that are effective against both gram-negative and gram-positive microorganisms. QAC salts have been recognized as amongst the best disinfectants and antibiotics for the fight against bacterial infections. The salts have different components, with almost similar functional groups.

Herein, we have synthesized six different benzalkonium salts via a one pot, two-step process via nucleophilic addition reaction followed by Menschutkin reactions. The compounds synthesized are: (1-(4-nonylphenoxy)-3-(2,6-dimethylpiperidinium chloro-1-yl)propan-2-ol); (1-(4-nonylphenoxy)-3-(2,6-dimethylpiperidinium bromo-1-yl)propan-2-ol); (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl) ammonium chloro)propan-2-ol); (1-(4-nonylphenoxy)-3-(N-benzyl-N-(1-phenylethyl)ammoniumbromide)propan-2-ol); (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenylammoniumbromo)propan-2-ol); (1-(3-nonylphenoxy)-3-(N-(2,4-dinitrophenyl)-N-phenyl ammonium chloro)propan-2-ol). The compounds were characterized using ^{1}H NMR, FT-IR spectroscopic techniques. The compounds are generally soluble in ethanol, ethyl ether, methanol, and chloroform at room temperature. They are generally stable up approximately to 206 °C.

The salts have potential applications as bactericidal and bacteriostatic antibiotic with good thermal stability. These potential antibacterial agents may thus, lead to reduced production cost. The potential exists for the compounds to be effective against current bacteria which have developed resistance to current drugs. Compounds could be effective against gram-negative bacteria and gram-positive bacteria.

The compounds are being studied for antibacterial activity. Future work will reveal the efficacy of these compound agents bacteria.

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